# Antibiotics Prescribing by General Practitioners for Urinary Tract Infections in Elderly Patients

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King's College London

# Antibiotics Prescribing by General Practitioners for Urinary Tract Infections in Elderly Patients

by

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**A thesis submitted in partial fulfilment of the requirements of King's College London for the degree of Doctor of Philosophy**

**September, 2016**

# Abstract

Urinary tract infections (UTIs) are the second most common infection seen by general practitioners (GPs) in the elderly. UTIs in the elderly can lead to serious complications with increased risk of mortality, yet there are no national or international dedicated guidelines for antibiotic treatment in this patient group. The epidemiology of UTIs in the United Kingdom (UK) for the elderly population and GPs' antibiotics prescribing for this condition have received little or no attention. This thesis describes GPs' antibiotics prescribing for UTIs in elderly patients in the UK by exploring the prevalence of UTIs in elderly patients, auditing GPs' antibiotics prescribing, explaining the variations in GPs' views and perceptions and identifying the factors that may influence or affect GPs' antibiotics prescribing using a mixed methods approach.

To achieve research aim, a comprehensive explanatory sequential mixed methods approach was undertaken. The initial research was quantitative and took the form of a retrospective, cross-sectional, drug utilisation study that included elderly patients' data retrieved from electronics medical records, namely, Disease Analyzer (IMS-DA), for the period between 1 January 2010 and 31 December 2012. The subsequent research was qualitative and took a phenomenographic approach with two analytical techniques: phenomenographic analysis and thematic analysis, with data collected through semi-structured interviews with 17 GPs.

The results from the quantitative study identified 77,290 UTI visits by 21,150 elderly patients, of whom 77.42% (N = 16,375) received at least one antibiotic prescription per visit over the study period. The mean age and sex adjusted UTI prevalence was found to be 23.35 (95% CI 21.84-24.85) per 1,000 person-years for year 2010, 21.44 (95% CI 19.99-22.88) per 1,000 person-years for year 2011 and 17.88 (95% CI 16.56-19.19) per 1,000 person-years. The total number of issued antibiotics prescriptions for UTIs during the study period was 37,815. Adherence results showed that 9,125 (24.1%) broad-spectrum antibiotics prescriptions were issued for elderly patients, including ciprofloxacin (N = 1,733; 4.6%), co-amoxiclav (N = 2,350; 6.2%) and cephalexin (N = 5,042; 13.3%). Additionally, 32.2% (N = 12,159) of antibiotics prescriptions were prescribed for durations other than those recommended either for treatment or for prophylaxis; this was seen in 10,605 (33%) female patients' UTI antibiotics prescriptions and 1,554 (27.5%) male patients' UTI antibiotics prescriptions. The findings from the qualitative study identified five distinct categories of description representing the ways in which GPs perceive antibiotics prescribing in elderly patients with UTIs. These categories are perceptions, knowledge, decision, practice and approach. Moreover, GPs' knowledge and perceptions about antibiotics were found to be shaped through seven external horizons: undergraduate education, postgraduate training, personal experience, interaction with peers, interaction and influence of patients' expectations, the healthcare system, and availability of guidelines and evidence. Additionally, the thematic analysis revealed 29 factors that may influence GPs' antibiotics prescribing for UTIs including: GPs' personal experience and familiarity with specific antibiotics, GPs' education, knowledge and training, complacency, GPs' fear, responsibility of other healthcare professionals, GPs' awareness about antibiotic resistance threat, GPs' awareness about microbial resistance results and information GPs' awareness about local resistance pattern, GPs' antibiotic prescribing concerns, diagnosis and clinical decision making by GPs', GPs' ethos and ethical values, patient's age and gender, patient's medical history and clinical characteristics, patient's social situation and living conditions, patient's level of understanding and knowledge, patient's desire for a quick fix, patient's autonomy, visits and education by prescribing advisors, audit, monitoring and feedback of prescribing, influence by secondary care doctor prescribing practice, implementation of local policies, guidance and formulary, time, guidelines and evidence, antibiotics shortage, incentives, media, cost, healthcare resources and constraints, pharmaceutical companies, over-prescribing and society experience and expectation.

In conclusion, the findings from the mixed methods research confirmed that some GPs in the UK are less likely to adhere to available good practice points for the management of UTIs in elderly patients, that there are variations among GPs' views and perceptions about antibiotics and that GPs' antibiotics prescribing practice is influenced by various factors such as guidelines, complacency, clinical presentation, resistance, and audit and feedback. The results highlight the need to optimise and rationalise GPs' antibiotics prescribing in the elderly by developing robust guidelines synthesised specifically for the elderly population based on studies and evidence from literature designed for elderly patients, to increase GPs' awareness of and familiarity with guidelines, to increase their uptake and involve GPs in the process of evidence synthesis because of their knowledge of the context of general practice. There is also a need to implement a multifaceted intensive approach with the aim of minimising variations in GPs' views for AMR and approaching elderly patients, modifying GPs' antibiotics perceptions and determining whether they will change their practice, correcting some GPs' misperceptions such as patients' expectations of antibiotics and patients' satisfaction through encouraging communication and targeting the GPs' seven external horizons through multifaceted educational programmes.

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# Acknowledgements

Thanks and praise be to ALLAH (GOD), who provided me with health, strength patience, knowledge and determination to complete this research work.

I would like to thank a number of people who, in one way or another, contributed to the completion of this thesis. I could have never made this journey without all the encouragement I have received along the way. I am most grateful to my supervisors, Dr Sue C Jones and Professor Paul F Long, for their invaluable guidance, patience, help, encouragement, advice, valuable comments and endless support since day one of this journey.

I want particularly to acknowledge Professor Mike Sharland, chair of the Department of Health's Expert Advisory Body on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI), as a field expert for his advice and suggestion of choosing this topic, and I thank him heartily. Many thanks to the following faculties and staff from University College London, Imperial College London and the University of Hong Kong for their special assistance in this thesis: Professor Ian Wong, Mr Kenneth Man and Mr Wallis Lau for their support they provided in data statistical analysis and revision; Dr Macey Murray for extracting data from IMS-Disease Analyzer; Dr Sonia Saxena and Dr Austen El-Osta for their assistance in the recruitment process. Also, I would like to thank Dr Charlotte Parker and Dr Kieran Hand for their time to take part in the pilot interview; Mrs Karen Poole, King's College London Library Information Specialist, for her assistance in confirming literature search for this thesis. I am very grateful to all of the general practitioners from all over the UK who contributed data to IMS-Disease Analyzer, without whom this study could not see the light. I also would like to extend my gratitude to all general practitioners for their contribution in the interviews used in this thesis. To my friends, in the United Kingdom and the Kingdom of Saudi Arabia who have supported me throughout the years and I am very grateful for their friendships, advices and support.

Also, I would like to express my great appreciation to the government of Kingdom of Saudi Arabia for their financial support, King Saud University for providing me with this opportunity to complete my PhD and Saudi Arabian Cultural Bureau in London for making this stage of my life so easy through providing me with the necessary administrative and logistic support.

Finally, I would like to express my gratitude to my father, mother, brothers and sisters. I can never thank you enough for all your love, continuous prayers and support throughout these years. In particular, I thank my father Abdulrahman for his faith in me and providing me with unending encouragement. The understanding shown by him during the years is greatly appreciated.

# Scientific Contribution

Parts of this thesis was presented at conferences:

**Workshop and Oral Presentation**

Alomar HA, Long P, Jones SC. (2015) Drug Utilisation Review (DUR) in Urinary Tract Infections (UTIs) from Epidemiological and Economical Perspectives. The Case of Antibiotics in Geriatric Patients. 1st International Conference of Clinical Pharmacy. Qassim, Saudi Arabia. 15-17 February, 2015.

**Poster Presentation**

Alomar HA, Long P, Jones SC. (2015) Antibiotic Prescribing for Urinary Tract Infections (UTIs) in Elderly Patients: General Practitioners' (GPs') Views and Perceptions. 1st International Conference of Primary Care and Public Health Medicine & 3rd International Congress of Person Centred Medicine. London, United Kingdom. 29-31 October 2015.

# Abbreviations

| Abbreviation | Meaning |
|---|---|
| ADRs | Adverse Drug Reactions |
| AMR | Antimicrobial Resistance |
| ANOVA | Analysis of variance |
| ASB | Asymptomatic Bacteriuria |
| AT | Anatomical Therapeutic |
| ATC | Anatomical Therapeutic Chemical |
| BIA | British Infection Association |
| BIOSIS | Biosciences Information Service |
| BMA | British Medical Association |
| BNF | British National Formulary |
| CCG | Clinical Commission Group |
| CDC | Centre for Disease Control and Prevention |
| CFU | Colony Forming Unit |
| CI | Confidence Interval |
| CINAHL | Cumulative Index of Nursing and Allied Health Literature |
| CKS | Clinical Knowledge Summaries |
| CNS | Central Nervous Systems |
| CPRD | Clinical Practice Research Datalink |
| CPSG | Clinical Prescribing Subgroup |
| CVA | Cerebrovascular Accidents |
| CVDs | Cardiovascular Diseases |
| CVS | Cardiovascular System |
| DDD | Defined Daily Dose |
| DM | Diabetes Mellitus |
| DOT | Days of Therapy |
| DUR | Drug Utilisation Research |
| *E. coli* | *Escherichia coli* |
| EAU | European Association of Urology |
| EMBASE | Excerpta Medica Database |
| EMRs | Electronic Medical Records |
| ePACT.net | Electronic Prescribing Analysis and Cost.net |
| E*ph*MRA | European Pharmaceutical Market Research Association |
| ESAC-Net | European Surveillance of Antimicrobial Consumption-Network |
| ESBL | Extended Spectrum Beta-Lactamase |
| ESCMID | European Society of Clinical Microbiology and Infectious Diseases |
| ESIU | European Section for Infections in Urology |
| ESPAUR | English Surveillance Programme for Antimicrobial Utilisation and Resistance |
| GFR | Glomerular Filtration Rate |
| G-I-N | Guidelines International Network |
| GIT | Gastrointestinal Tract |
| GP surgeries | General Practice Surgeries |
| GPRD | General Practice Research Database |
| GPs | General Practitioners |
| HCPs | Healthcare Professionals |
| HMIC | Health Management Information Consortium |
| HRA | Health Research Authority |
| HSCIC | Health and Social Care Information Centre |
| HSE | Hospital Episode Statistics |
| IDSG | Interdepartmental Steering Group on Antimicrobial Resistance |
| IMS Health | Intercontinental Marketing Services Health |
| IMS-DA | Intercontinental Marketing Services Disease Analyzer |

| Abbreviation | Meaning |
|---|---|
| INPS | In-Practice Systems |
| INR | International Normalisation Ratio |
| IOM | Institute of Medicine |
| IPA | International Pharmaceutical Abstracts |
| ISEAC | Independent Scientific and Ethical Advisory Committee |
| KAP | Knowledge, Attitudes and Practices |
| KCL | King’s College London |
| KPC | *Klebsiella pneumoniae* carbapenemase |
| LOT | Length of Therapy |
| MDRGNB | Multiple-Drug-Resistant Gram-Negative Bacilli |
| MEDLINE | National Library of Medicine |
| MeSH | Medical Subject Heading |
| MRSA | Methicillin-Resistant Staphylococcus Aureus |
| MSU | Midstream Urine |
| NHS | National Health Service |
| NHS-BSA | National Health Service-Business Services Authority |
| NICE | National Institute for Health and Care Excellence |
| NRES | National Research Ethics Service |
| NTRAG | North Thames Research Appraisal Group |
| OCLC | Online Computer Library Center |
| OOH | Out-of-hour |
| OTC | Over-the-counter |
| PD | Pharmacodynamic |
| PHE | Public Health England |
| PK | Pharmacokinetic |
| PRSP | Penicillin-Resistant Streptococcus Pneumoniae |
| RCGP | Royal College of General Practitioners |
| RCTs | Randomised Controlled Trials |
| RTIs | Respiratory Tract Infections |
| SACAR | Specialist Advisory Committee on Antibiotic Resistance |
| SAPG | Scottish Antimicrobial Prescribing Group |
| SD | Standard Deviation |
| SIGN | Scottish Intercollegiate Guidelines Network |
| SMC | Scottish Medicines Consortium |
| SPDR | Swedish Prescribed Drug Register |
| SPSS | Statistical Package for the Social Sciences |
| TARGET | Treat Antibiotics Responsibly, Guidance, Education, Tools |
| THIN | The Health Improvement Network |
| TMP-SMX | Trimethoprim-Sulfamethoxazole |
| UA | Urinalysis |
| UCL | University College London |
| UK | United Kingdom |
| USA | United States of America |
| UTIs | Urinary Tract Infections |
| VAMP | Value Added Medical Products |
| VRE | Vancomycin-Resistant Enterococci |
| WBCs | White Blood Cells |
| WHO | World Health Organization |
| WIC | Walk-in-centre |
| WWII | World War II |

# Glossary

| Term | Definition |
|---|---|
| ***Adverse drug reaction*** | A response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for modification of physiological function (Cluff *et al.* 1972, p. 9). |
| ***Ageing*** | Chronological age, that is, time elapsed since birth; and any person aged 65 years or over is often referred to as ‘elderly’ (Orimo 2006, Shi *et al.* 2008, WHO 2010, Singh and Bajorek 2014). |
| ***Antibiotics*** | Chemical substances which have the capacity to inhibit the growth and even to destroy pathogenic organisms (Waksman 1952, p. 370). |
| ***Antimicrobial resistance*** | The is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it (Ashiru-Oredope *et al.* 2014, p. 6). |
| ***Antimicrobial stewardship*** | An organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness (Cefai *et al.* 2015, p. 7). |
| ***Appropriate antibiotic use CPSG*** | The use of antimicrobials in the most appropriate way for the treatment or prevention of human infectious diseases, having regard to the diagnosis (or presumed diagnosis), evidence of clinical effectiveness, likely benefits, safety, cost (in comparison with alternative choices), and propensity for the emergence of resistance. The most appropriate way implies that the choice, route, dose, frequency and duration of administration have been rigorously determined (Clinical Prescribing Subgroup 2001, p. 8). |
| ***Appropriate antibiotic use WHO*** | The cost-effective use of antimicrobials which maximises their clinical therapeutic effect, while minimising both drug-related toxicity and the development of antimicrobial resistance (Stamm *et al.* 2001, p. 15). |
| ***Broad-spectrum antibiotics*** | Antibiotics that target many pathogens (Genao and Buhr 2012, Murray *et al.* 2013b). |
| ***Co-morbidity*** | Combination of additional diseases beyond an index disorder (Marengoni *et al.* 2011, p. 430). |
| ***Confirmability*** | Objectivity (neutrality) and the control of researcher bias (Lincoln and Guba 1985, Ritchie *et al.* 2014). |
| ***Credibility*** | A quality assessment of whether the data convincingly describe the phenomenon under investigation (Lincoln and Guba 1985, Ritchie *et al.* 2014). |
| ***Days of therapy*** | Number of days that a patient receives a certain antibiotic, independently of the quantity and used doses (Grau *et al.* 2013, Schechner *et al.* 2013, WHO Collaborating Centre 2015). |
| ***Defined daily dose*** | The assumed average maintenance dose per day for a drug used for its main indication in adults (Grau *et al.* 2013, Schechner *et al.* 2013, WHO Collaborating Centre 2015). |
| ***Dependability*** | A concept of consistency of the findings when the research replicated (Lincoln and Guba 1985, Ritchie *et al.* 2014). |
| ***Drug utilisation review WHO*** | Studies or research related to marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences (Birkett *et al.* 2003, p. 8). |
| ***Drug utilisation review North America*** | Research or studies related to the prescribing, dispensing and ingesting of drugs (Brodie 1971, p. 1). |
| ***Epistemology*** | The manner by which knowledge is constructed and the relationship of the knower to the known (Guba and Lincoln 1994, p. 108). |
| ***External horizon*** | The way in which the phenomenon is delimited from and related to its context (Barnard *et al.* 1999, p. 216). |
| ***General practice*** | First level contact with people to improve health in a community. In a system with a gatekeeper, all initial (non-emergency) consultations with doctors, nurses or other health staff (Lakhani *et al.* 2007, p. 4). |
| ***General practitioners*** | Personal doctors, primarily responsible for the provision of comprehensive and continuing generalist care to every individual seeking medical care irrespective of age, sex and state of health (Lakhani *et al.* 2007, p. 4). |

| Term | Definition |
|---|---|
| ***Generalisability*** | A term concerned with the extent to which research findings can be relevant beyond the setting and context in which they were generated, that is, outside the sample in which the research was conducted (Lincoln and Guba 1985, Mays and Pope 2000). |
| ***Grey literature*** | Literature which is produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publisher (Farace and Frantzen 1998, p. iii). |
| ***Hawthorne effect*** | A phenomenon where a study subject's behaviour and/or study outcomes are altered as a result of the subject's awareness of being under observation (Mangione-Smith *et al.* 2002, p. 1604). |
| ***Human behaviour*** | The collective range of behaviours performed by humans, influenced by a number of factors such as attitudes, culture, ethics, emotions, values, rapport, authority, persuasion, coercion and/or genetics; while the way a human being acts is determined more by their attitudes, genetics, core faith and social norms (Ajzen 2005). |
| ***Internal horizon*** | How component parts of the phenomenon are understood and are related to each other (Barnard *et al.* 1999, p. 216). |
| ***Length of therapy*** | Number of days that a patient receives an antibiotic irrespective of the number of different drugs (Grau *et al.* 2013, Schechner *et al.* 2013, WHO Collaborating Centre 2015). |
| ***Literature review*** | The comprehensive study and interpretation of literature that relates to a particular topic (Aveyard 2014, p. 1). |
| ***Macro-level factors*** | Factors related to society, national or international context (Watt *et al.* 2007, p. 29). |
| ***Meso-level factors*** | Factors related to practice or CCG context (Watt *et al.* 2007, p. 29). |
| ***Methodological approach*** | Framework that brings together broad research assumptions into a detailed plan, data collection method(s), analysis of data and interpretation of research findings (Harwell 2011, Creswell 2014). |
| ***Micro-level factors*** | Factors related to individual GP and patient interaction context (Watt *et al.* 2007, p. 29). |
| ***Mixed methods*** | Class of research where the researcher mixes or combines quantitative and qualitative research techniques, methods, approaches, concepts or language into a single study. Mixed methods research also is an attempt to legitimate the use of multiple approaches in answering research questions, rather than restricting or constraining researchers' choices (i.e., it rejects dogmatism).<br>It is an expansive and creative form of research, not a limiting form of research. It is inclusive, pluralistic, and complementary, and it suggests that researchers take an eclectic approach to method selection and the thinking about and conduct of research (Johnson and Onwuegbuzie 2004, pp. 17-18). |
| ***Multi-morbidity*** | The coexistence of multiple chronic diseases (Marengoni *et al.* 2011, p. 430). |
| ***Narrow-spectrum antibiotics*** | Antibiotics that target a limited range of pathogens (Genao and Buhr 2012, Murray *et al.* 2013b). |
| ***Ontology*** | The nature of reality (Guba and Lincoln 1994, p. 108). |
| ***Outcome space*** | A graphical, hierarchical presentation of findings which consists of a related set of a finite number of categories of description that collectively expresses the variety of ways in which the phenomenon under study is experienced by a group of individuals in a given context, that is, real world (Åkerlind 2005). |
| ***Patterns of antibiotic use*** | The extent and profiles of antibiotic use and the trends in antibiotic use over time (Birkett *et al.* 2003). |
| ***Perception*** | An individual's or group's unique way of viewing phenomena, involving the processing of stimuli and incorporate memories and experiences in the process of understanding. (McDonald 2012, p. 8). |
| ***Pharmacoepidemiology*** | The study of the use and effects/side-effects of drugs in large numbers of people with the purpose of supporting the rational and cost-effective use of drugs in the population thereby improving health outcomes (Birkett *et al.* 2003, p. 8). |

| Term | Definition |
|---|---|
| ***Phenomenographic analysis*** | A qualitative analysis in which data is analysed and discussed from a second-order perspective that described how the phenomenon was viewed and understood by the participants rather than how it was understood by the researcher (Marton and Booth 1997). |
| ***Phenomenography*** | A research method for mapping the qualitatively different ways in which people experience, conceptualise, perceive, and understand various aspects of, and various phenomena in, the world around them (Marton 1986, p. 31). |
| ***Polypharmacy*** | Quantitative: Concurrently taking two or more drugs for 240 days or more; or administering at least two to nine drugs concurrently (Veehof *et al.* 2000).<br>Qualitative: The prescription, administration or use of more drugs than are clinically indicated in a given patient (Montamat and Cusack 1992). |
| ***Prescribed daily dose*** | The average dose prescribed according to a representative sample of prescriptions (Grau *et al.* 2013, Schechner *et al.* 2013, WHO Collaborating Centre 2015). |
| ***Prevalence*** | Measures of all cases in the population who have the disease within a specified time frame (Kier 2011, p. 12). |
| ***Prudent prescribing of antibiotics*** | Prudent (or optimal) use meant both ‘less’, there still being leeway to reduce unnecessary use, and ‘appropriate’ (not only the right antibiotic but also the right dose, administered by the most appropriate route and for the right length of time to effect a clinical cure, while minimising side effects and the development of resistance) (Clinical Prescribing Subgroup 2001, p. 8). |
| ***Qualitative research*** | A broad term used to describe a wide range of diverse research approaches in respect to research aims, theoretical assumptions, understanding of phenomenon under investigation, methodological focus and the methods they apply (Flick *et al.* 2004). |
| ***Recruitment*** | The process whereby the researcher identifies and invites (recruits) participants to join the study (Given 2008, p. 743). |
| ***Recruitment adequacy*** | Sufficient, relevant data being generated through the participants (Bassett 2004). |
| ***Recruitment appropriateness*** | Selecting participants with relevant experience and knowledge to inform the research (Bassett 2004). |
| ***Thematic analysis*** | Independent qualitative and descriptive method that is mainly used to identify, analyse and report patterns, that is, themes, within data in nuanced and rich details (Braun and Clarke 2006, p. 79). |
| ***Transferability*** | Whether the descriptions and interpretations in the study are useful in other contexts (Lincoln and Guba 1986, Guba and Lincoln 1992). |
| ***Triangulation*** | The process of combining different study groups, methods, temporal and local settings, and different theoretical perspectives in dealing with a phenomenon. As a strategy, triangulation aims to promote and improve the quality of qualitative research, that is, reliability and validity (Flick 2009). |
| ***UTIs*** | The presence and multiplication of microorganism(s), in one or more structures of the urinary tract, with associated tissue invasion (Cowling *et al.* 2014, p. 8). |

# Chapter 1 Introduction

## 1.1 Introduction

This chapter consists of four sections that together represent a general overview of the research topic. Of the sections, the first provides a brief overview of primary care and general practitioners (GPs) in the United Kingdom (UK); the second outlines the behaviours and problems associated with GPs' antibiotics prescribing, along with antibiotics consumption in primary care; the third focuses on age-related changes and infectious diseases as well as antibiotics use in the elderly; and the fourth gives general information about urinary tract infections (UTIs) in the elderly.

## 1.2 UK Primary Care and the GP Workforce

### 1.2.1 Definitions and Responsibilities

In the UK, general practice surgeries (GP surgeries) are the first point of access to healthcare (Kennedy et al. 2011). The Royal College of General Practitioners (RCGP) defines general practice as:

> *'First level contact with people taking action to improve health in a community. In a system with a gatekeeper, all initial (non-emergency) consultations with doctors, nurses or other health staff'* (Lakhani *et al.* 2007, p. 4);

whereas GPs are:

> *'Personal doctors, primarily responsible for the provision of comprehensive and continuing generalist care to every individual seeking medical care irrespective of age, sex and state of health'* (Lakhani *et al.* 2007, p. 4).

One of a UK GP's core duties – alongside offering patient consultations, referrals, screening, immunisation, managing long-term conditions and promoting health – is safely prescribing drugs to patients if needed (Lakhani *et al.* 2007).

In the UK, any person wanting to become a GP[1] must go through a five-year undergraduate programme in medical school followed by a two-year foundation level

[1]The terms 'GP', 'doctor', 'family medicine' and 'physician' are different and have specific definitions. However, they are often used interchangeably in the relevant literature. Thus, in this thesis they are used interchangeably to refer to GPs.

programme, then a three-year postgraduate course, with 18 months spent in hospitals seeing a wide range of acute conditions at first hand and the other 18 months spent in one or two general practices (Knowles and Bliss 2014). GPs as healthcare professionals (HCPs) have a mindset centred on patients' best care by considering patients as priorities and providing excellent quality care (Papanikitas and Toon 2011). In general practice, ethos and values are usually strong and GPs tend to have an open-ended relationship with their patients, many of whom are different generations of the same families (Cocksedge *et al.* 2011).

Although there is no accurate official number, it was estimated that approximately 98% of the total UK population (N > 59 million) are registered with primary care GPs under the National Health Service (NHS), through which the medical services provided are mostly free of charge (Baker 2011, HSCIC 2012). The rest of the population may not be registered with a GP owing to special situations such as being homeless, a prisoner or a member of the armed forces (Lawrenson *et al.* 1999).

### 1.2.2 GPs Workforce in the UK

There are 43,009 practising GPs, excluding locums, working in 9,783 GP surgeries across the UK's (BMA 2014). The majority of practising GPs in the UK (N = 26,236, 61%) are female. It is estimated that 340 million consultations are undertaken every year with people seeing their GP six times a year on average, which is double the number of visits from the previous decade (BMA 2014). Every day, more than 800,000 people are seen in GP surgeries by either GPs or practice nurses. In 2014, the estimated average time a GP spent with each patient was 12 minutes (Knowles and Bliss 2014).

Figure 1 illustrates the 2013 GP workforce distributed across the UK's four nations. This number of GPs is insufficient to cope with the current challenges including financial viability, declined income, GPs quitting the profession, increased workload, demand for superior care quality and time pressures that potentially prevent GPs from making informed decisions, particularly for an ageing population with complex health conditions (BMA 2014). Therefore, the quality of services provided, including prescribing, are likely to become compromised negatively as a result of this shortage and high demand. A recently published British Medical Association (BMA) survey of 2,830 GP surgeries across England showed that 1,202 (46%) had GPs in their workforce (N = 294, 10%) who were intending to leave the UK because they believe it to be financially 'unsustainable' (BMA 2016).

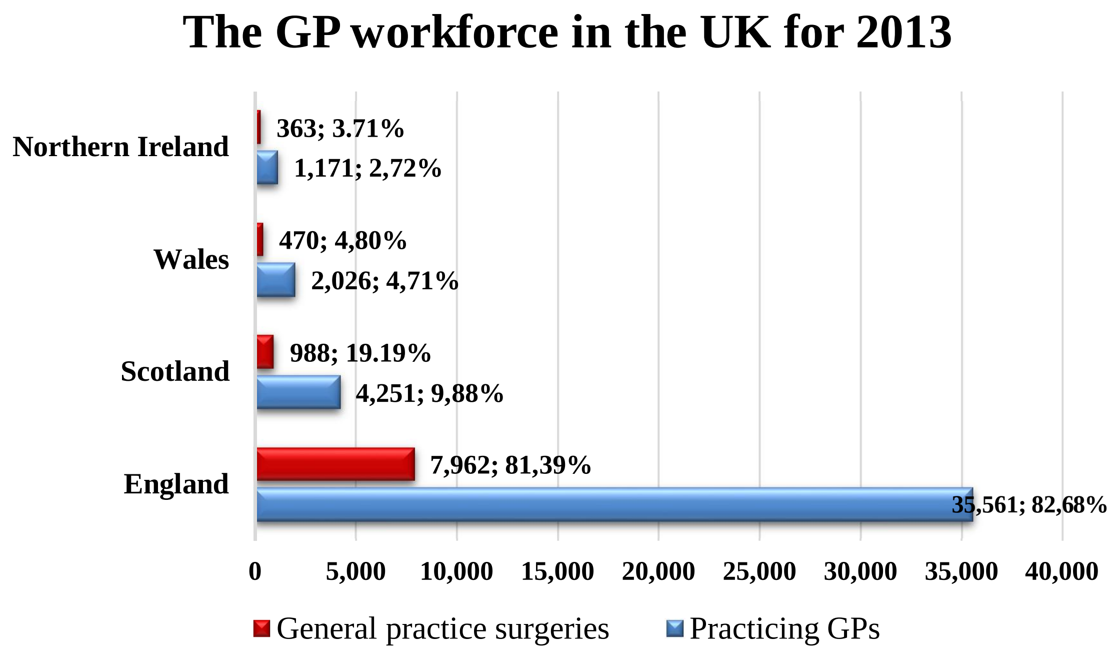


Figure 1: Number of practising GPs and GP surgeries in the UK in 2013 (BMA 2014)

## 1.3 Antibiotics

There is no doubt that the introduction of antibiotics in 1941 revolutionised medicine; it was one of the landmark advances in clinical practice of modern medicine (Powers 2004). Worldwide, infections such as pneumonia, diphtheria, tuberculosis and diarrhoea were the main causes of death in children and adults during the 19th century (Zaffiri *et al.* 2012). The discovery and introduction of antibiotics to treat infections allowed for such a remarkable increase in human life expectancies that, in 1967, William Stewart, the Surgeon General of the United States of America (USA), said:

> *'It is time to close the book on infectious diseases, and declare the war against pestilence won'* (Martinez and Baquero 2014, p. 68).

Furthermore, the added value of antibiotics for prophylactic and therapeutic purposes was so persuasive that many older antibiotics never underwent any randomised controlled clinical trials (RCTs) to assess their efficacy and safety (Hulscher *et al.* 2010).

The term *'antibiotics'* was first used in literature by American biochemist and microbiologist Selman Waksman, in 1942, to describe a substance produced by an organism known as *Actinomyces antibioticus* with the capability to kill and inhibit the growth of bacteria (Waksman and Tishler 1942). Later, during his inaugural speech at the Nobel Prize awards ceremony in 1952, he defined antibiotics as:

> *'Chemical substances which have the capacity to inhibit the growth and even to destroy pathogenic organisms'* (Waksman 1952, p. 370).

Originally, the word 'antibiotic[2]' was coined to describe compounds with antimicrobial properties that come from natural sources, such as specific strains of fungus or bacteria, as opposed to 'antibacterial', which was used to describe synthetic compounds with similar activity. However, antibiotics no longer refers only to compounds from natural origin (Pelaez 2006).

### 1.3.1 Historical Overview

The history of antibiotics was linked to several scientists including Paul Ehrlich, Alexander Fleming, Gerhard Domagk, Howard Florey, Ernst Chain and Selman Waksman (Aminov 2010). All of these received Nobel Prize, the most prestigious awards for intellectual achievement in the world, for their valuable contributions to the discovery and development of antibiotics (Nobelprize.org 2007a, Nobelprize.org 2007b, Nobelprize.org 2007c).

In 1904, Paul Ehrlich, a German bacteriologist, introduced the concept of the *'magic bullet'*, which was based on laboratory observation. It described how a substance can selectively target or attack only the microorganisms that cause diseases but not the host. This observation led him to start a series of large-scale, systematic screening trials to find a drug that was active against *Treponema pallidum*, a syphilis-causing microorganism that was widespread and incurable at that time. He and his colleagues discovered the first chemical cure for syphilis in 1909 (Strebhardt and Ullrich 2008).

Then, in 1928, Scottish bacteriologist and immunologist Alexander Fleming left uncovered culture plates of *Staphylococci* in the laboratory of Saint Mary's Hospital in London whilst he went on holiday. When he returned, he noticed that many culture plates were contaminated with a mould that had produced a yellow substance, which in turn had created what appeared to be a zone of lysed bacteria, that is, it had inhibited the bacterial

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[2] The terms 'antibacterials', 'antibiotics' and 'antimicrobials' are different and have specific definitions. However, they are often used interchangeably in the relevant literature. Thus, in this thesis they are used interchangeably to refer to natural and synthetic compounds that target bacteria.

growth. Fleming consequently investigated this phenomenon by culturing the mould, which he later described as *Penicillium notatum*, and successfully isolating an active substance that had the ability to inhibit bacterial growth. He called it penicillin (Hoff *et al.* 2008).

In 1932, Gerhard Domagk, a German pharmacologist, started testing the antibiotic properties of a red dye used to colour cloths and known as prontosil red, because of its brilliant colour. Gerhard discovered that this dye was capable of curing *Streptococcal* infections in mice. Through doing this, he discovered sulphanilamide, a sulphonamide compound produced as a result of prontosil dye metabolism. In 1943, Domagk's six-year-old daughter became seriously sick because of infection with a *Streptococcal* microorganism. Her desperate father injected his daughter with prontosil, thus saving her from arm amputation and death (Iyer 2008, Maruta 2009).

Taking matters further still, in 1940, Australian pathologist Howard Florey, with the assistance of Ernst Chain, a German chemist, successfully extracted, purified and described the protocol for penicillin production. This led to penicillin being produced in commercial quantities to treat infections in injured soldiers during World War II (WWII). These soldiers were among the first people in history to benefit from antibiotics, and thousands of young soldiers' lives were saved (Kardos and Demain 2013).

In 1943, Selman Waksman, an American biochemist and microbiologist, discovered streptomycin while screening soil-derived *Streptomycetes* for their antimicrobial activities against a susceptible test microorganism by detecting zones of growth inhibition on an overlay plate. Waksman's assistants, Elizabeth Bugie and Albert Schatz, performed preliminary investigations on streptomycin and results showed that it had antibiotic activity against a wide range of bacteria including *Mycobacterium tuberculosis*, which causes tuberculosis infection (Woodruff 2014). Figure 2 illustrates the timeline for the discovery, market introduction and resistance development of antibiotics over the years.

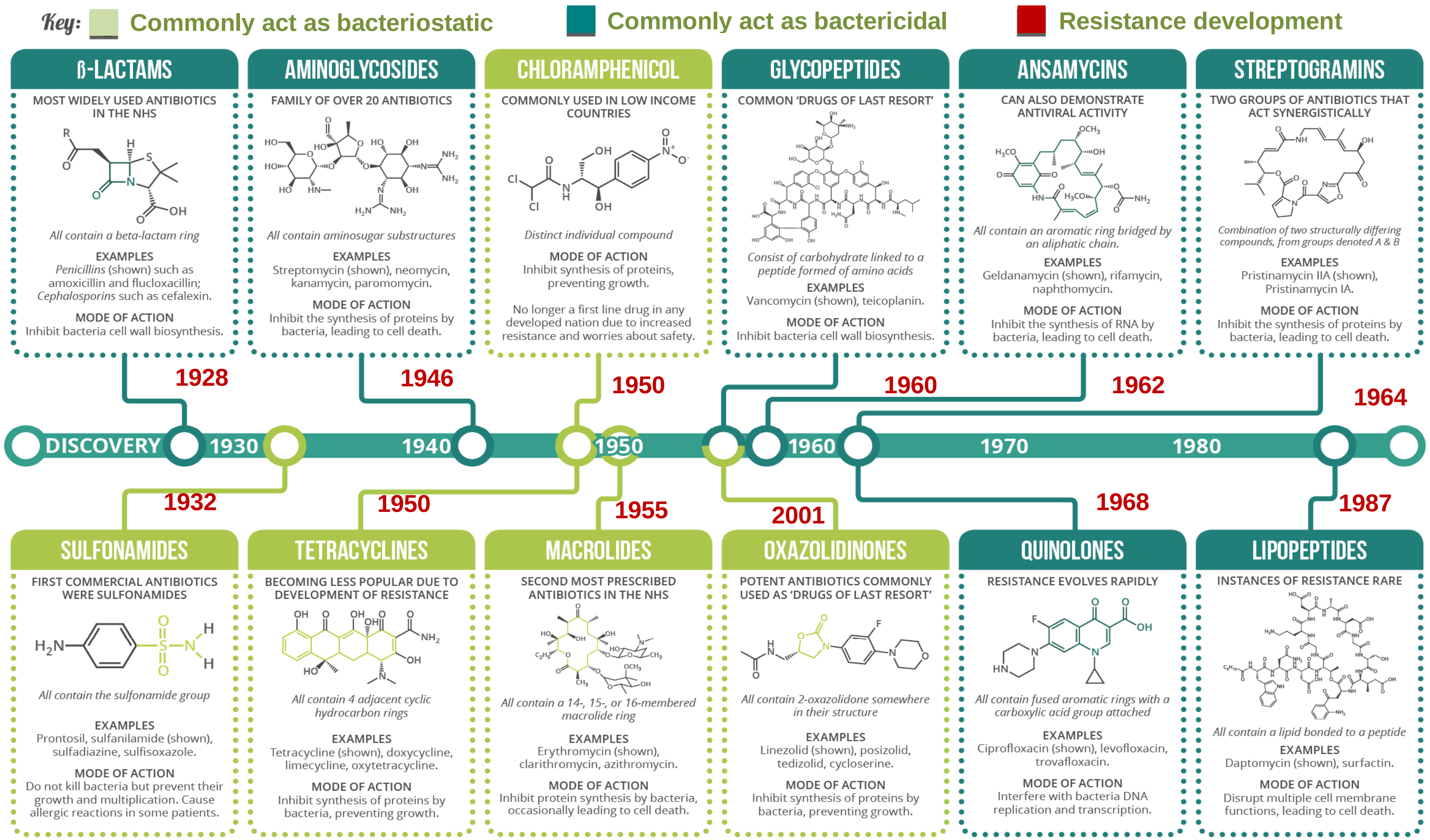



Figure 2: Antibiotics discovery, market introduction and resistance development timeline and classification according to chemical structure, activity and site of action (Compound Interest 2014)

### 1.3.2 Current Overview

Demand for new generations of antibiotics to replace the old, relatively ineffective ones has increased dramatically in recent years. However, the development pipeline is strained, with only a few novel classes of antibiotics – glycylcycline, lipopeptide, pleuromutilin, novel glycolipopeptide, macrocyclic and diarylquinoline – having been marketed since 2000 (Butler *et al.* 2013, Laxminarayan 2014). Unfortunately, none of these new classes targets bacterial strains, which are often deadly such as *Klebsiella pneumoniae* carbapenemase (KPC) and known to adapt more readily to antibiotics (Renwick *et al.* 2016). In 2015, a new antibiotic class known as teixobactin was discovered in the USA (Piddock 2015). Although it has been found to be active against many bacteria such as *Staphylococcus aureus*, *Clostridium difficile*, *Bacillus anthracis* and *Mycobacterium tuberculosis*, it is still at an early stage of development and there are no guarantees that it will reach the market (Piddock 2015). There are currently at least 19 antibiotics in clinical development in the European Union (UN) and the USA, although there is no known development timeline for these (Renwick *et al.* 2016).

### 1.3.3 Antibiotics Classification

More than 100 antibiotics have been identified since the discovery of penicillin, which has led to the creation of a more practical and convenient method for classifying antibiotics. As any classification system can provide researchers and HCPs with a framework for remembering and understanding the use of different agents (Goering *et al.* 2012), it was necessary to highlight some key terms that will be used frequently in this thesis.

The first classification system was based on antibiotic chemical structure alone, which had no place in practice because of the diversity of this method. However, when chemical structure is combined with the antibiotic site of action it provides a useful working classification. The key groups in this classification are beta-lactam, macrolides, lincosamides, aminoglycosides, tetracyclines, polypeptides, sulphonamides, fluoroquinolones and miscellaneous (Genao and Buhr 2012, Murray *et al.* 2013b). A second classification system was based on antibiotic spectrum of activity, which can be either narrow or broad depending on the number of different bacterial species against which they exert their activity (Genao and Buhr 2012, Murray *et al.* 2013b). A third classification system was based on antibiotic site of action, which was considered more convenient than using chemical structure. Antibiotics can exert action on cell wall synthesis, protein synthesis, nucleic acid synthesis, metabolic pathways and cell membrane function. Other classifications that may be used to describe antibiotics include route of administration, for example whether oral or parenteral, and type of activity, which can be either bactericidal, that is, it kills the infecting microorganisms directly, or bacteriostatic, that is, it inhibits the growth and replication of the infecting pathogens and limits the spread of infection, allowing the immune system to eliminate the bacteria (Genao and Buhr 2012, Murray *et al.* 2013b). Figure 2 illustrates examples of antibiotic groups classified according to activity type and chemical structure.

### 1.3.4 Antibiotics Use and Resistance

Unlike other drugs, antibiotics act on living pathogens, rather than on just the patient (Zaffiri *et al.* 2012). This has caused bacteria to evolve and develop traits that enable them to survive exposure to antibiotics, that is, antimicrobial resistance (AMR) (Smith *et al.* 2014), which can be defined as:

> *'Resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it'* (Ashiru-Oredope *et al.* 2014, p. 6)

Alexander Fleming predicted resistance in 1945 when he received his Nobel Prize for discovering penicillin. During the award ceremony he delivered a lecture to the audience in which he stated:

> *'The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily under-dose himself and by exposing his microbes to nonlethal quantities of the drug make them resistant'* (Fleming 1945b, p. 83).

Fleming's increasing worries about resistance made him repeat his warning every time he gave a speech or interview as if he felt strongly that this was an upcoming threat, for example when he stated:

> *'The public will demand penicillin…then will begin an era…of abuses. The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out which can be passed to other individuals and perhaps from there to others until they reach someone who gets a septicaemia or a pneumonia which penicillin cannot save. In such a case the thoughtless person playing with penicillin treatment is morally responsible for the death of the man who finally*

> *succumbs to infection with the penicillin-resistant organism. – I hope the evil will be averted .'*(Fleming 1945a, p. 21).

Resistance is a natural phenomenon and it can be either clinical, resulting from an inadequate level of antimicrobial concentration within the tissue or fluid, or microbiological, where the pathogen possesses a resistant mechanism (Blair *et al.* 2015). The latter can be divided into either intrinsic (primary) or acquired (secondary) and is determined genetically by pathogen characteristics that include the cell wall, enzymes and biochemistry (Blair *et al.* 2015).

In the past two decades, AMR has increased dramatically to the extent where it has created the fear that the world might return to the era of pre-antibiotics (Tomaras and Dunman 2015). This rise in AMR was a result of several factors such as reduction in the development of novel antibiotics by many large pharmaceutical companies because of both the low return on investment, since they are prescribed for short duration and have the potential to lose their activity owing to resistance, and the implementation of antimicrobial stewardship programmes that keep the new antibiotics in reserve. In addition, research and development of new antibiotics is more expensive because of complicated regulatory requirements. Moreover, the new screening methods for possible compounds have not been as successful as was expected (MacGowan and Macnaughton 2013). Other reasons for the increase in AMR include overuse or misuse of antibiotics in human as well as increased use of antibiotics in food industry, veterinary medicine and for growth promotion and disease prevention in agriculture (Laxminarayan *et al.* 2013).

Recently, Public Health England (PHE) report for combined antibiotic use in humans and animals in the UK showed that the total UK antibiotics use across humans and animals was 949.9 tonnes of active ingredients in 2013, with 531.9 tonnes (56%) used by humans alone (Borriello *et al.* 2015). Analysis of IMS (Intercontinental Marketing Service) Health sales data aimed at estimating global human antibiotics consumption from 2000 through 2010, combining direct sales data from manufacturers and indirect sales data from wholesalers to estimate the total volume of antibiotics sold in hospitals and retail pharmacies in 71 countries including the UK, showed an increase of 36%, from approximately 4,083,964,813 standard units[3] to 73,620,748,816 standard units (van Boeckel *et al.* 2014).

[3] The number of sold doses. A dose can be a pill, a capsule or an ampoule.

Relating to humans, several studies (Steinke *et al.* 2001, Goossens *et al.* 2005), a meta-analysis (Bell *et al.* 2014) and a systematic review (Costelloe *et al.* 2010) have linked the emergence of AMR with excessive antibiotics consumption, exposure and overall uptake of antibiotics. Additionally, antibiotics misuse and overuse have been identified as key drivers for AMR in a systematic review (Kardas *et al.* 2005). Moreover, the link between level of antibiotics prescribing and prevalence of AMR has been recognised at the individual (Costelloe *et al.* 2010), general practice (Schmiemann *et al.* 2012) and country-wide level (Goossens *et al.* 2005).

The impact of AMR can be catastrophic and should not be underestimated as it can lead to several negative consequences such as increased length and severity of infection experienced by individuals, spread of infection, limited use of techniques that require infection control, use of alternative antibiotics with lesser-known safety profiles, increased financial cost of treatment and care, increased morbidity and increased time off work (Maragakis *et al.* 2008, Llor and Bjerrum 2014). A technical report by the European Centre for Disease Prevention and Control (ECDC) showed that AMR was responsible for almost 400,000 patients getting infected with multiple drug resistance bacteria and about 25,000 patient deaths each year (Norrby *et al.* 2009). Furthermore, the report estimated the annual cost associated with AMR to be at least €1.5 billion on extra healthcare costs and productivity losses alone. If complications associated with AMR are considered, the estimated annual cost can jump to €9 billion just within Europe (Verhoef *et al.* 2005).

If the current AMR scenario continues to rise, it is estimated that it will lead to the death of 300 million people over the next 35 years, with expected financial losses, in terms of economic output, of $60 trillion to $100 trillion (Taylor *et al.* 2014). A recently published governmental report by the Cabinet Office showed that the UK government also expects a dramatic increase in AMR over the next 20 years. Furthermore, if this increase in resistance becomes an outbreak, almost 200,000 people will be affected by bacterial blood infection that might not respond effectively to the currently available antibiotics and might cause the death of 80,000 people (Cabinet Office 2015).

To assist in the reduction of these negative consequences of resistance, the UK government has therefore developed a five-year AMR strategy with the overarching aim of slowing the development and spread of AMR by focusing on three strategic aims:

improving the knowledge and understanding of AMR; conserving and stewarding the effectiveness of existing treatments; and stimulating the development of new antibiotics, diagnostics and novel therapies (Davies and Gibben 2013).

### 1.3.5 Inappropriate Antibiotic Prescribing in Primary Care

The efficacy of currently available antibiotics is fading just when practitioners are facing serious mounting issues relating to antibiotics. Many practitioners even prescribe antibiotics to patients using the maxim *'It cannot hurt'* meaning that, even if it does not exert an action as intended, the risk of harm is relatively minimal (McDonnell Norms Group 2008). This mistaken perception is probably because of antibiotics use coming at no cost to either patients or society (McDonnell Norms Group 2008). Other factors such as HCPs' attitudes, patients' satisfaction, demands and expectations (Lopez-Vazquez *et al.* 2012, Teixeira Rodrigues *et al.* 2013, Teixeira Rodrigues *et al.* 2016) as well as end of patency of most antibiotics, making them cheaper owing to the availability of several generic preparations, have resulted in increased inappropriate antibiotics prescribing, neglecting the fact that they can cause harm (Ebert 2007, Powers 2009). Worldwide, it was found that around 20%–50% of antibiotics were prescribed inappropriately or unnecessarily (Tonna 2009, Ashiru-Oredope *et al.* 2012).

The World Health Organization (WHO) defined appropriate antibiotics use as:

> *'The cost-effective use of antimicrobials which maximises their clinical therapeutic effect, while minimising both drug-related toxicity and the development of antimicrobial resistance'* (Stamm *et al.* 2001, p. 15).

In the UK, the Clinical Prescribing Subgroup (CPSG) of the Interdepartmental Steering Group on Antimicrobial Resistance (IDSG) defined appropriate antimicrobial use as:

> *'The use of antimicrobials in the most appropriate way for the treatment or prevention of human infectious diseases, having regard to the diagnosis (or presumed diagnosis), evidence of clinical effectiveness, likely benefits, safety, cost (in comparison with alternative choices), and propensity for the emergence of resistance. The most appropriate way implies that the choice, route, dose, frequency and duration of administration have been rigorously determined* (Clinical Prescribing Subgroup 2001, p. 8).

Furthermore, the CPSG steering committee, has introduced the following statement to describe the prudent prescribing of antibiotics:

> *'In line with this definition, the CPSG considered that prudent (or optimal) use meant both 'less', there still being leeway to reduce unnecessary use, and*

> *'appropriate' (not only the right antibiotic but also the right dose, administered by the most appropriate route and for the right length of time to effect a clinical cure, while minimising side effects and the development of resistance).'* (Clinical Prescribing Subgroup 2001, p. 8).

Unlike the WHO definition, the CPSG definitions were comprehensive and covered all aspects of antibiotic use. Moreover, the definitions provided an insight into how appropriate antibiotics use can be a multifaceted and intricate process integrating both the decision and the selection in the prescribing process.

In general, it is clear that appropriate use of antibiotics does not simply mean that all antibiotics prescribing should be widely and blindly reduced. Although withholding antibiotics is prudent if they are not clinically indicated, there are many circumstances in which they are. Linking between falls in antibiotics prescribing for some infections can cause death owing to pneumonia, for instance (NHS 2003). Even when antibiotics are clinically indicated they are sometimes prescribed and used inappropriately. Therefore, GPs must satisfy several important criteria before they can consider their prescribing to be appropriate (Slama *et al.* 2005, Leekha *et al.* 2011). Table 1 summarises appropriate prescribing criteria as well as the common forms of inappropriate prescribing in clinical practice.

Table 1: Summary of criteria for appropriate antibiotics prescribing and some common forms of inappropriate antibiotics prescribing in clinical practice

| Criteria for appropriate antibiotics prescribing (Slama *et al.* 2005, Leekha *et al.* 2011) | Common forms of inappropriate antibiotics prescribing (Leekha *et al.* 2011, McCoy 2013) |
|---|---|
| ▪ Accurate diagnosis<br>▪ Understand the difference between empiric and definitive therapy<br>▪ Select the appropriate dosage, route, interval and identify when to switch to narrow-spectrum, cost-effective oral agent for the shortest duration necessary<br>▪ Understand drug characteristics factors that are peculiar to antimicrobial agents<br>▪ Consider patient's characteristics factors which might influence antibiotic activity<br>▪ Recognise the adverse effects of antibiotics on the patient | ▪ Prescribing antibiotics for non-bacterial infections<br>▪ Not prescribing antibiotics for infections that require treatment<br>▪ Prescribing expensive antibiotics compared with a similar spectrum agent<br>▪ Prescribing too broad-spectrum antibiotics; prescribing too narrow-spectrum antibiotics; prescribing for too long or too short a duration<br>▪ Prescribing an inappropriate route<br>▪ Prescribing an inappropriate dose |

In primary care, prescribing practice can be challenging since it involves autonomy – of GPs, especially with regards to decision-making, on one hand and of patients, in terms of having the right to make their own medical decisions, without the influence of any HCPs on the other (Stiggelbout *et al.* 2004). However, this can creates ethical dilemmas over which takes priority, which sometimes exposes patients to higher risk of complications, longer illness duration and increased risk of mortality if the expected benefit of antibiotics therapy is not sufficiently substantial (Littmann and Viens 2015).

In the UK, GPs are regularly blamed for inappropriate antibiotics prescribing and there have been many calls to penalise ‘soft-touch’ GPs who prescribe too many antibiotics (McCartney 2015, NICE 2015a). Professor Mark Baker, director of the Centre for Clinical Practice at the National Institute for Health and Care Excellence (NICE), UK, highlighted on GPs’ inappropriate antibiotics prescribing when he stated:

> *'In England, GPs are responsible for 10 million inappropriate prescriptions each year’* (NICE 2015a).

Results from a Longitude Prize[4] survey of 1,004 GPs across the UK showed that 49% (N = 492) admitted to prescribing antibiotics at least once a week without knowing whether they were necessary, 45% (N = 452) prescribed antibiotics for viral infections knowing that they would not be effective, 44% (N = 444) prescribed antibiotics to get a patient to leave the consulting room and 72% (N = 723) prescribed antibiotics despite being unsure whether the infection was bacterial or viral. Moreover, 90% (N= 904) of GPs said they feel under pressure to prescribe antibiotics (NESTA poll 2014) and 97% of patients who requested antibiotics get them (McNulty *et al.* 2013). This irrational prescribing is likely to aggravate the growing AMR crisis and threaten both healthcare and the public.

Increased inappropriate antibiotics prescribing by GPs has led many governmental organisations within the UK, such as NICE, PHE and RCGP, to develop a wealth of initiatives and interventions targeting GPs with the aim of increasing the appropriateness of antibiotics prescribing in part through changing GPs’ knowledge, attitudes and practices (Harris 2013). One of the most important interventions was developing of antibiotics prescribing stewardship competence programmes, which refer to:

> *‘An organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness’* (Cefai *et al.* 2015, p. 7).

[4] A national science prize in which the public vote for the most pressing issue facing humanity.

This was achieved through the implementation of the Treat Antibiotics Responsibly, Guidance, Education, Tools (TARGET) Antibiotics Toolkit resources programme, which was developed through PHE and RCGP collaboration and launched in November 2012. TARGET resources included local and national guidance on antibiotics treatment recommendations, educational materials and tools GPs can share with patients during consultations including information on expected duration of infection, self-care and back-up prescriptions and suggested antibiotics practice audits. TARGET materials were updated in 2013 following preliminary users testing and evaluation (Ashiru-Oredope *et al.* 2016).

Another intervention included appointing prescribing advisors, mainly pharmacists with specialised knowledge of drugs and prescribing issues in primary care (Pinder *et al.* 2015). These pharmacists were employed by the local Clinical Commission Group (CCG) mostly to support and advise GPs on all aspects of drugs prescribing and the therapy process to promote rational prescribing with improved pharmaceutical care, promoting patient safety, ensuring that GPs adherence to local formularies and curbing prescribing cost (Duerden *et al.* 2011). Prescribing advisors have made considerable efforts in recent years to steer GP choice away from broad-spectrum antibiotics such as quinolones and cephalosporins, which has resulted in significantly reduced *Clostridium difficile* infection and resistance owing to these drugs (Ashiru-Oredope *et al.* 2012).

A third intervention involved auditing of antibiotic prescribing with feedback. For many years, audit and feedback was used widely to promote the implementation of research evidence and evaluate the quality of antibiotics prescribing by comparing GPs' prescribing patterns with guidelines and peers (Pinder *et al.* 2015). Audit and feedback was found to be one of the most effective methods of encouraging behaviour change, according to a NICE guide aimed at encouraging HCPs to change their practice to improve patient care (Eccles *et al.* 2007). Auditing activity is usually carried out by a prescribing advisor or a medicine management team, either pharmacist-led or GP-led, and can include all aspects of the supply and use of drugs, from individual drug reviews to health promotion programmes (Blenkinsopp and Bond 2008), on behalf of GP surgeries, particularly those participating in antibiotics incentive scheme or known for over-prescribing behaviour. The number of performed audits may be subject to time availability as it is a labour-intensive process and could require educational feedback on over-prescribing (McNulty and Francis 2010). It was found that delivering audit feedback to GPs individually can influence their prescribing on a personal or local level. However, to extend the influence to the macro-level, a national feedback action must be carried out to disseminate key messages to as many GPs as possible (Watt *et al.* 2007). The impact of national feedback was reported to substantially reduce antibiotics prescribing at low cost as it was evident by a recently published RCT in the UK aimed to reduce unnecessary prescriptions of antibiotics by GPs in England. (Hallsworth *et al.* 2016).

A fourth intervention included antibiotics incentive scheme that focused on linking payments to the achievement of previously set targets designed to reward and motivate GPs to achieve higher levels of performance and improve prescribing cost-effectiveness (Mason *et al.* 2005, Goodwin *et al.* 2011). This is usually done by examining the total number of antibiotics items and the number of broad-spectrum antibiotics prescribed by GPs participated in the scheme in relation to patient population. This incentive has been found to improve antibiotics prescribing, reduce prescribing cost and change GPs' prescribing behaviour (McNulty and Francis 2010). Recently, NHS England launched the world's largest healthcare incentive scheme to reduce the number of antibiotics prescribed in primary care by 4%, or to the average performance levels of 2013/14, by supporting each CCG with up to £150,000 a year (NHS 2016).

Additional activities included European Antibiotic Awareness Day, which falls on 18 November each year, the Antibiotic Guardian pledge campaign, to slow resistance and cut unnecessary use of antibiotics and antibiotics prescribing leads (Harris 2013, Pinder *et al.* 2015). Moreover, these organisations have encouraged all GPs to get involved in educational and training programmes, use local and national guidelines, delayed prescribing approach, use the decision support system, pathways and tools, and enhance communication skills with patients (Harris 2013, Llor and Bjerrum 2014, Pinder *et al.* 2015).

### 1.3.6 GPs' Antibiotics Prescribing Behaviour

GPs' prescribing behaviour is a very broad concept that incorporates a variety of dimensions. To date, there is no precise consensus on the definition of behaviour (Stålsby Lundborg and Tamhankar 2014). Human behaviour might describes the collective range of behaviours performed by individual, influenced by a number of factors such as attitudes, culture, ethics, emotions, values, rapport, authority, persuasion, coercion and/or genetics; while the way a human being acts is determined more by their attitudes, genetics, core faith and social norms (Ajzen 2005).

In practice, the decision to prescribe antibiotics is made during consultation with a patient. The process of prescribing an antibiotic is not a simple one-way process from GP to patient; rather, it is the result of considering complex behavioural interactions among different stakeholders, including the GP, the patient and the healthcare system (Ranji *et al.* 2006, Lopez-Vazquez *et al.* 2012, Teixeira Rodrigues *et al.* 2013). In the UK, Bradley (1992) conducted a qualitative interview study in northern England to explore the discomfort experienced by 74 GPs in relation to decisions about whether or not to prescribe. The findings revealed that GPs consider antibiotics prescribing one of the most uncomfortable prescribing decisions they make owing to pharmacological reasons such as toxicity and efficacy and non-pharmacological reasons such as workload, anger and ignorance (Bradley 1992).

GPs' antibiotics prescribing behaviour can be influenced by a number of factors – on five main ecological levels – emphasising the interaction between, and interdependence of, factors within and across all levels of a health problem as highlighted by literature (Rimer and Glanz 2005, Teixeira Rodrigues *et al.* 2013, Stålsby Lundborg and Tamhankar 2014). Moreover, some of these factors can be changed or modified through changing GPs' behaviour, as shown by a qualitative semi-structured interview study of 18 UK GPs (Armstrong *et al.* 1996). These ecological levels are: 1) individual-level knowledge, attitudes, beliefs and personality, for example prescribing in case of diagnostic uncertainty; 2) interpersonal-level social identity, for example GP–patient relationship; 3) institutional-level rules, guidelines, regulations and informal structures; 4) community-level social networks and norms, for example, prescribing liberally or restrictively; and 5) public policy-level regulations and laws, for example restricting policy on antibiotics (Stålsby Lundborg and Tamhankar 2014). In the literature, factors that influence antibiotics prescribing were grouped contextually into intrinsic factors (GPs' knowledge, attitudes and socio-demographics) and extrinsic factors (patients, the pharmaceutical industry and the healthcare system) as it was shown in two systematic reviews one for qualitative literature (Teixeira Rodrigues *et al.* 2016) and one for quantitative literature (Lopez-Vazquez *et al.* 2012). Table 2 summarises the intrinsic and extrinsic factors that affect GPs' antibiotics prescribing behaviour, as in-depth understanding these is essential for combating inappropriate antibiotics prescribing, minimising AMR and designing effective interventions (Tonkin-Crine *et al.* 2015, Teixeira Rodrigues *et al.* 2016). A systematic review by Arnold and Straus (2005) showed that the effectiveness of any intervention to improve antibiotics prescribing depends on physicians' behaviour and the barriers within the community setting (Arnold and Straus 2005). Since exploring the factors influencing GPs' antibiotics prescribing practice in UTIs is one of this thesis' main objectives, the factors are discussed in more detail in Chapter Two.

Table 2: Summary of the intrinsic and extrinsic factors that influence GPs' antibiotics prescribing behaviour(Lopez-Vazquez *et al.* 2012, Teixeira Rodrigues *et al.* 2013)

| | **Intrinsic factors** | |
|---|---|---|
| **GP's socio-demographic** | **GP's attitudes**[5] | **GP's knowledge** |
| ▪ Age<br>▪ Gender<br>▪ Medical specialty<br>▪ Previous clinical experience<br>▪ Years of practice<br>▪ CME<br>▪ Medical school and residency | ▪ Complacency[6]<br>▪ Fear[7]<br>▪ Ignorance[8]<br>▪ Indifference[9]<br>▪ Responsibility of others[10]<br>▪ Confidence[11] | ▪ Awareness of evidence regarding antibiotics efficacy<br>▪ Awareness of resistance and over-prescribing<br>▪ Awareness of guideline |
| | **Extrinsic factors** | |
| **Patient** | **Healthcare system** | **Pharmaceutical industry** |
| ▪ Age<br>▪ Gender<br>▪ Race<br>▪ Socio-economic status<br>▪ Signs and symptoms<br>▪ Clinical condition<br>▪ Co-morbidities<br>▪ Anxiety<br>▪ Patient demand<br>▪ Educational level<br>▪ Desire to have a speedy recovery<br>▪ Type of medical insurance | ▪ Communication and organisational model<br>▪ Time pressure<br>▪ Workload<br>▪ Ownership of the practice location<br>▪ Type & location of the healthcare centre<br>▪ Private or public<br>▪ Accreditation level<br>▪ Implemented policies and guidelines<br>▪ Cost savings and financial incentives | ▪ Prescribing pressure |
| CME: Continuing Medical Education | | |

Each of these factors plus others such as the influence of the media (Hawkings *et al.* 2007, Lambert *et al.* 2007, Holloway 2011) and society's experience and expectations

[5] A general feeling or evaluation – positive or negative – about some person, object or issue (Hogg and Vaughan 2014, p. 136).
[6] Attitude that motivates the prescribing of antibiotics to fulfil professionals' perceptions of their patients'/parents' expectations.
[7] Attitude relating to fear of possible future complications in the patient and/or fear of losing patients.
[8] Lack of relationship between over-prescribing and antibiotic resistance, linked to lack of knowledge.
[9] Lack of motivation to feel positively or negatively inclined to the problem of antibiotic prescribing.
[10] Attitude underlying the belief that responsibility for generating antibiotic resistances lies other professionals.
[11] Describe the self-reliance felt by physicians when prescribing antibiotics.

(McDonnell Norms Group 2008) belong to one of the three levels of the healthcare system paradigms – the macro (national/international) level, the meso (CCG and practice) level or the micro (GP–patient) level – or they can operate across all three levels as shown in Figure 3 which illustrates the factors that can impact prescribing across the healthcare system level (Watt *et al.* 2007).

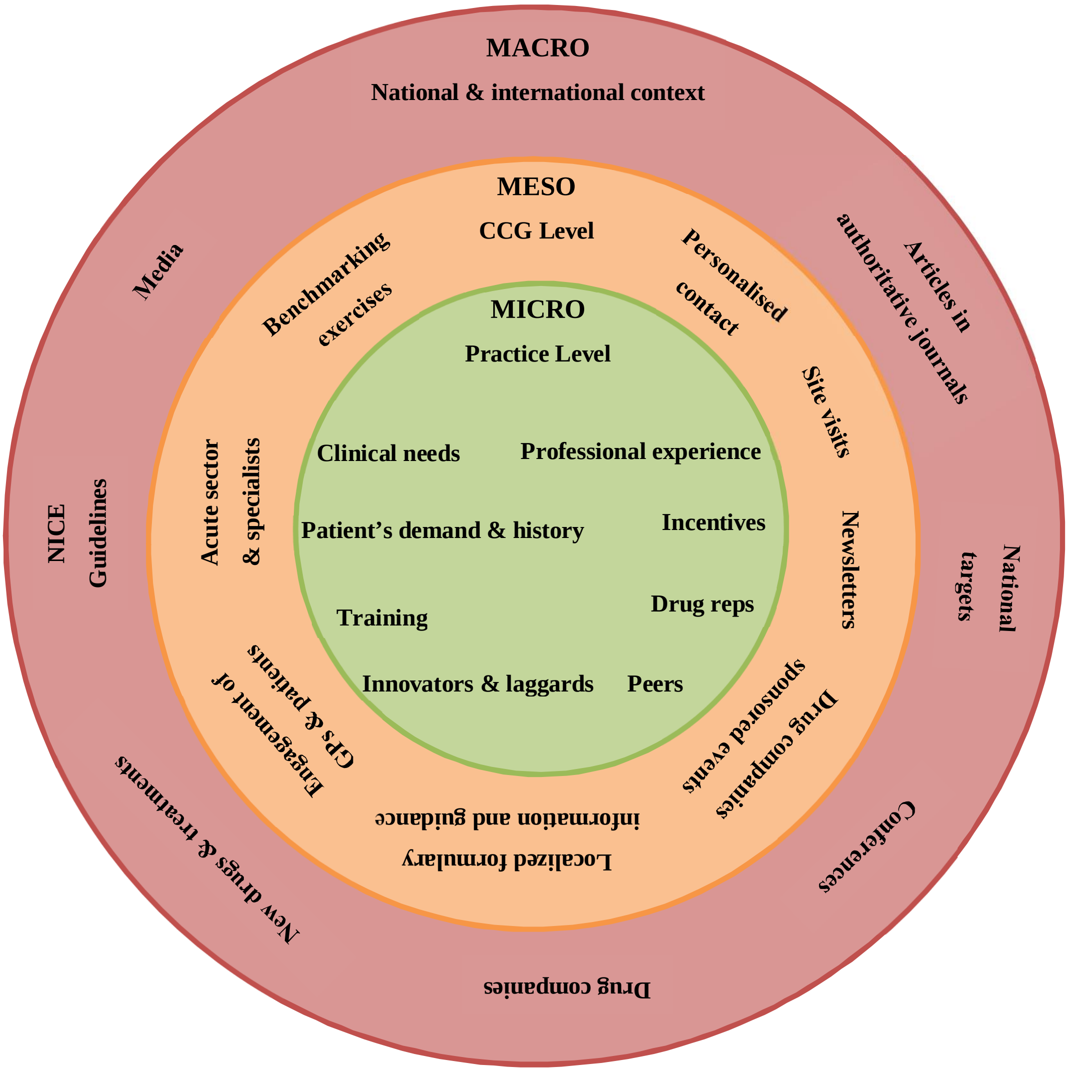
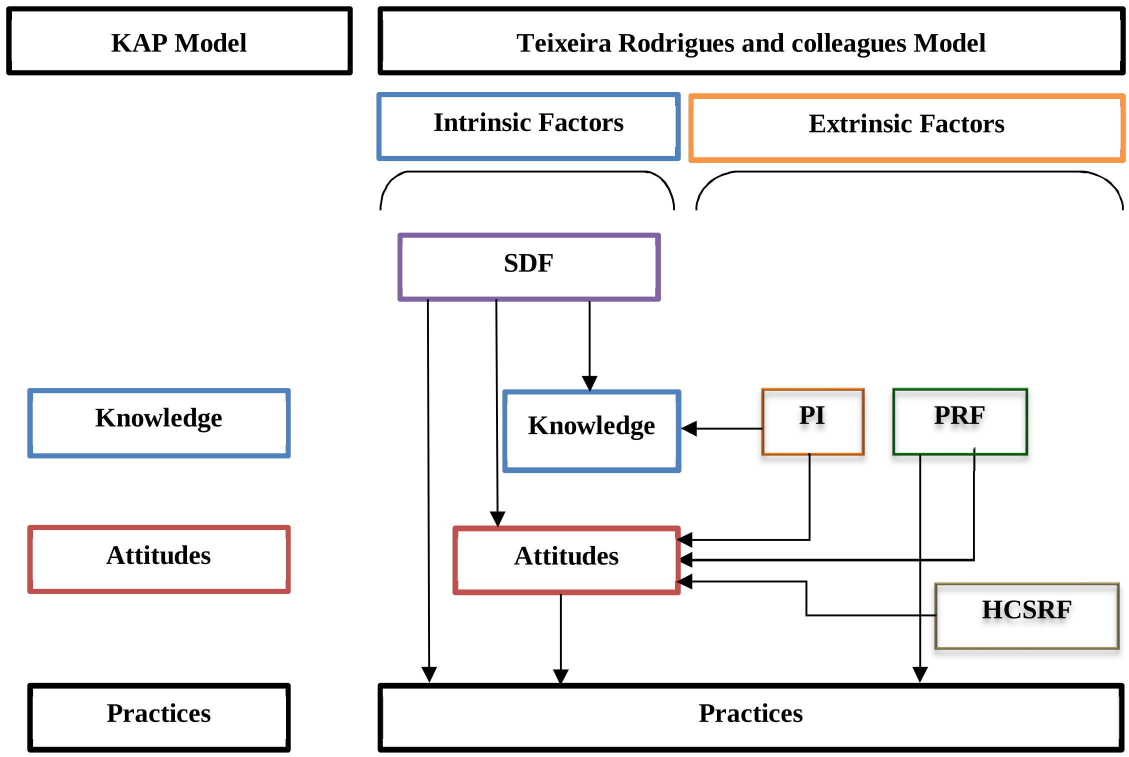



Figure 3: Factors influencing GPs' prescribing behaviour at the macro, meso and micro levels of the healthcare system (Watt *et al.* 2007, p. 10)

These factors in addition to the previously highlighted challenges may aggravate the status of inappropriate antibiotics prescribing and spread AMR by preventing GPs from prescribing antibiotics more prudently. Furthermore, no theoretical framework model has been able to describe the interrelationships among these factors. As a result, no one has been able to explain why the different interventions implemented such as GPs education and training, diagnostic testing and restriction policies have not been as effective as was hoped (Lopez-Vazquez *et al.* 2012). A recent theoretical framework for structuring the interrelationships among the factors was proposed by Teixeira Rodrigues *et al*. (2013), as shown in Figure 4. This framework was based on the original knowledge, attitudes and practices (KAP) model, which was developed in the 1950s to explain what is known, believed and done in relation to a particular topic, to explain the possible interrelationships. However, this framework was not validated.




**SDF: Sociodemographic factors**
**PI: Pharmaceutical industry**
**PRF: Patient related factors**
**HCSRF: Healthcare system related factors**

Figure 4: Proposed theoretical framework of interrelationships among factors influencing antibiotics prescribing (Teixeira Rodrigues *et al*. 2013, p. 210)

On the contrary, Stålsby Lundborg and Tamhankar described the interrelationships between these factors using the word *'chaos'* owing to the lack of a structured interrelated framework (Stålsby Lundborg and Tamhankar 2014). This means that the problem of inappropriate antibiotics prescribing is much more difficult than it seemed and might need multifaceted interventions and strategies that incorporate all of these multiple, independent interrelationship factors to resolve it. Changing GPs' antibiotics prescribing behaviour is a challenging mission; however, facilitating the process of behavioural change in addition to using multifaceted behavioural science interventions seems to be a feasible approach (Stålsby Lundborg and Tamhankar 2014, Pinder *et al*. 2015).

### 1.3.7 Antibiotics Consumption in UK Primary Care

AMR was found to be driven by the volume of antibiotics use, regardless of whether such use is appropriate or not (Goossens *et al.* 2005, Laxminarayan and Heymann 2012). Therefore, it is crucial to understand how antibiotics use is reported and what the sources of reporting are for antibiotics consumption.[12] Information on antibiotics consumption in primary care is of great importance to those HCPs and policy-makers in developing strategies to rationalise antibiotics use and slow the development of resistance, monitoring progress towards a more prudent use of antibiotics, benchmarking comparisons and evaluating the outcomes of antibiotics stewardship programmes and interventions (Aarestrup *et al.* 2014, Weist *et al.* 2014).

Antibiotics use can be measured with metrics that reflect an aggregate or average amount of antibiotics being consumed at the level of the patient, a unit or service, an entire institution or at the national level (Morris 2014). They consist of a numerator and a denominator, for example, a unit of measure per 1,000 inhabitants per day. Table 3 summarises the measurement units commonly used to report antibiotics consumption, with their advantages and disadvantages. Monitoring of consumption is usually presented in combination with a consumption period, for example annual; a setting, for example primary care; an indication, for example UTIs; and a level of data aggregation, for example trimethoprim (Grau *et al.* 2013, Schechner *et al.* 2013).

These metrics can be used to describe the amounts of ordered antibiotics, dispensed antibiotics and administered antibiotics, benchmarking and the ecological impact of antibiotics use on resistance (Ibrahim and Polk 2014). The most widely used and accepted unit of measurement for antibiotics consumption is defined daily dose (DDD), which was developed in the 1970s and has been further refined and promoted by WHO methodology (WHO Collaborating Centre 2015). However, owing to its lack of clinical relevance, it should not be used to evaluate the impact of antimicrobial stewardship strategies. Days of therapy (DOT) offers more clinical relevance to the healthcare provider than does DDD (Morris 2014).

[12] 'Use' and 'consumption' are used interchangeably to reflect the same meaning.

Table 3: Summary of measurement units commonly used to report antibiotics consumption with advantages and disadvantages (Grau *et al.* 2013, Schechner *et al.* 2013, WHO Collaborating Centre 2015)

| Measurement unit | Advantages | Disadvantages |
|---|---|---|
| Defined Daily Dose (DDD):<br>*The assumed average maintenance dose per day for a drug used for its main indication in adults* | ▪ Common and easy to collect<br>▪ Allows benchmarking between drugs and settings | ▪ Subject to bias when dose differs significantly from the reference value<br>▪ Longitudinal comparisons difficult owing to WHO continuous revision for reference values<br>▪ Some WHO reference values differ from the typically prescribed dose |
| Prescribed Daily Dose (PDD):<br>*The average dose prescribed according to a representative sample of prescriptions* | ▪ Adjusted to the real situation of the setting or type of patient | ▪ Not standardised<br>▪ Does not allow for benchmarking between different settings |
| Days of Therapy (DOT):<br>*The number of days that a patient receives a certain antibiotic, independently of the quantity and used doses* | ▪ Accurate estimation of multiple drug therapy<br>▪ Not influenced by discrepancy between DDD and PDD<br>▪ Can be used in children<br>▪ Independent of DDD changes | ▪ Patient-level data are needed<br>▪ Does not reflect the given dose |
| Length of Therapy (LOT):<br>*The number of days that a patient receives an antibiotic irrespective of the number of different drugs* | ▪ Accurate estimation of duration of therapy<br>▪ Not influenced by discrepancy between administered drugs which makes it suitable for children | ▪ Patient-level data are needed<br>▪ No reflection of multiple therapy<br>▪ No reflection of the dosage given<br>▪ Cannot be used to compare usage of individual drugs |

WHO: World Health Organisation

In the UK, information about antibiotics consumption can be obtained from different local, national and international sources, sorted into primary care, secondary care or both according to the setting and level of consumption required (Ashiru-Oredope *et al.* 2014). The first source is the Electronic Prescribing Analysis and Cost database (ePACT.net), which was established by the NHS-Business Services Authority (NHS-BSA) in 1988 to provide primary care prescriptions data without patients' specific information at local and national levels. Recently, the system was upgraded to provide secondary care data as well. This database provides information about all dispensed NHS prescriptions by community pharmacists, GPs, nurses and dentists from all over the UK. Information about costs and volumes from this database can be used for benchmarking between different organisations (Ballarín *et al.* 2015). However, these data have many limitations such as lack of indication records for which each antibiotic was prescribed, missing patients' gender and age information and inability to estimate what proportion of patients received prescriptions (Hayward *et al.* 2007).

A second source is the European Surveillance of Antimicrobial Consumption-Network (ESAC-Net). This is a Europe-wide network of national surveillance systems that includes 29 EU countries for community data and 18 countries for hospital data and is coordinated by the ECDC. ESAC-Net was launched in 2001 to monitor antibiotics consumption in community and hospital care using standardised data. The network publishes a variety of reports on subjects related to the prevention and control of communicable diseases as well as annual surveillance and consumption reports (ECDC 2015). One of the main drawbacks of these data is their inability to provide individualised hospital consumption information. A key advantage for these data is their ability to provide community consumption information that is adjusted for regional population size (ECDC 2015).

A third source is the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR). This programme was established by PHE in 2013 in response to the threat posed by AMR, as highlighted in the 2011 annual report of the UK Chief Medical Officer (Davies 2013) and as part of the UK's five-year strategy for tackling AMR (Davies and Gibben 2013). The main aim of this programme was to monitor antimicrobial utilisation and resistance in both primary and secondary care, and to monitor any unintentional clinical outcomes of future antimicrobial stewardship and behaviour change interventions, that is, to act as a benchmark for organisations to compare their quality measures and methods against regional and national standards (Ashiru-Oredope and Hopkins 2013).

In September 2015, NHS England and the Health and Social Care Information Centre (HSCIC) introduced a newer GP record and monitoring system known as care.data. This system had the ability to link patients' data from GP record systems with hospital data for secondary uses. Data from this system included patients' demographics, clinical information, prescribing data and referrals (Barr 2015). However, the release of this system was associated with debate about patients' information security and ethics associated with patients' data sharing without obtaining their own consent (Barr 2015). Owing to this debate and recommendation by a recent report published by the National

Data Guardian for Health and Care, NHS England has made the decision to shut down the system permanently (Freeman 2016).

All these sources have numerous advantages such as identifying trends in antibiotic resistance, assessing the magnitude of new resistance threats, following the dynamics of resistance trends, detecting new resistance mechanisms, monitoring the impact of empirical prescribing and generating consumption and surveillance reports (Critchley and Karlowsky 2004). However, none of these sources can record or document the proportion of antibiotics prescriptions that was actually administered by patients (Shallcross and Davies 2015). Perhaps one reason for this is the lack of infrastructure for measuring it, especially with patients' poor compliance (Morris 2014).

A recently published antimicrobial utilisation and resistance surveillance report by PHE showed that the total measured consumption of antibiotics in England in 2013 was 27.4 DDD per 1,000 inhabitants per day. The highest consumption was reported in GP surgeries (79%); and the individual prescription items of antibiotics for GP surgeries numbered 1.9 items per 1,000 inhabitants per day (Ashiru-Oredope *et al.* 2014). To translate this number to prescriptions, it is equivalent to 41.6 million antibiotics prescriptions at a cost to the NHS of £192 million (HSCIC 2014b) compared with 39.2 million antibiotics prescriptions during 2007 (HSCIC 2008). Figure 5 illustrates the number of antibiotic items dispensed in UK primary care between 2004 and 2014. It shows that both penicillin and macrolide consumption increased up to 2012 but decreased in 2013. Nitrofurantoin consumption increased 41% between 2010 and 2013 owing to its use for UTI, which was the largest increase observed. Broad-spectrum antibiotics such as ciprofloxacin and cephalexin decreased, though amoxicillin-clavulanic acid (co-amoxiclav) demonstrated a significant increase, which increases the risk of *Clostridium difficile* infection.

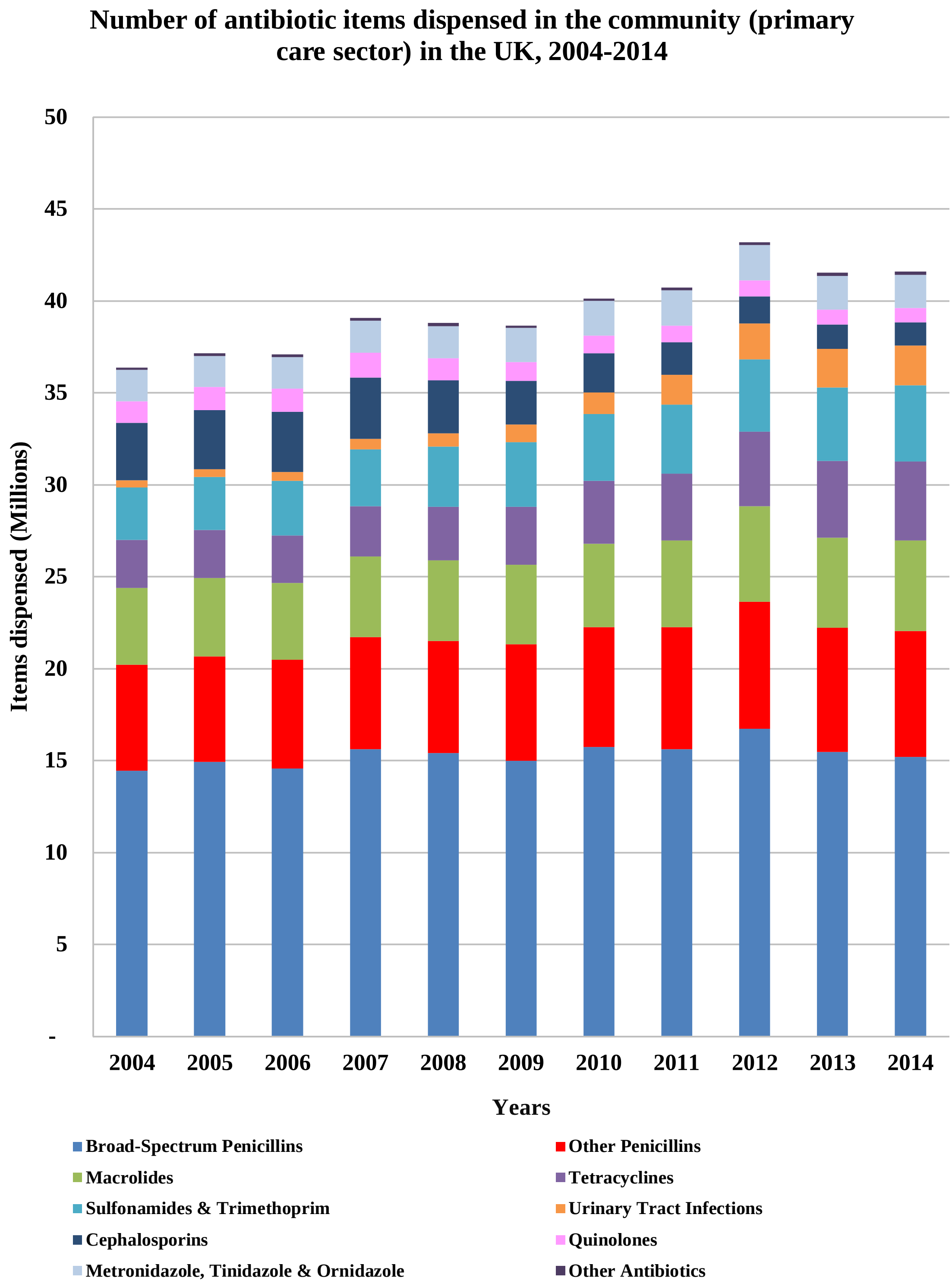



Figure 5: Number of antibiotic items dispensed[13] in the community between 2004 and 2014 (HSCIC 2015)

However, this figure may be underestimating the true consumption because it was generated from a surveillance system that lacks consumption data from the private

[13] Prescriptions dispensed in the community by community pharmacists and dispensing doctors in the UK. Both dispensed and consumed antibiotics reflect the same figures by two different reporting sources.

sectors. Furthermore, an increase of 4% in antibiotics consumption in GP surgeries between 2010 and 2013 was also reported without knowledge of the exact causes behind it. Proposed explanations for this increase include a higher number of patients presenting with infections and requiring antibiotic therapy and GPs over-prescribing antibiotics (Ashiru-Oredope *et al.* 2014).

Additionally, the report mentioned that only 15 antibiotics represented 98% of the total antibiotics consumption via GP surgeries in England. Table 4 lists the top 15 antibiotics prescribed in general practice in England in 2013. The trend of these items prescribing shows a decrease in broad-spectrum antibiotics ciprofloxacin and cefalexin, but a significant increase in co-amoxiclav. The findings from this report might suggest that bacteria that used to be sensitive to these antibiotics might become resistant in the future if the consumption continues to increase. Furthermore, caution is needed when interpreting the relative changes in consumption of each antibiotic as an increase in one antibiotic may cause a reduction in another, where an alternative drug is used for the same clinical indication (Ashiru-Oredope *et al.* 2014).

Table 4: Ranks and relative consumption of the top 15 consumed agents in general practice in England, 2013 (Ashiru-Oredope *et al.* 2014)

| **Antibiotic** | **Rank** | **Proportion of all antibiotic** | **Relative to 2010** |
|---|---|---|---|
| Amoxicillin | 1 | 29.3% | − |
| Clarithromycin | 2 | 7.9% | ↑ |
| Doxycycline | 3 | 7.9% | ↑ |
| Lymecycline | 4 | 7.9% | ↑ |
| Flucloxacillin | 5 | 7.2% | ↑ |
| Trimethoprim | 6 | 6.4% | ↑ |
| Erythromycin | 7 | 6.1% | ↑ |
| Co-amoxiclav | 8 | 6.0% | ↑ |
| Phenoxymethylpenicillin | 9 | 5.3% | ↑ |
| Oxytetracycline | 10 | 4.2% | ↓ |
| Nitrofurantoin | 11 | 3.8% | ↑ |
| Azithromycin | 12 | 1.8% | ↑ |
| Ciprofloxacin | 13 | 1.5% | ↓ |
| Cephalexin | 14 | 1.5% | ↓ |
| Metronidazole | 15 | 0.7% | − |

**−:** No change; ↑: Increased; ↓: Decreased

Shallcross and Davies reported that there is marked variation in antibiotics prescribing and consumption across the UK with some practices prescribing at double the rate of low-prescribing practices. For instance, in England there was consistently higher consumption of antibiotics in the northern regions compared with the southern regions (Shallcross and Davies 2014). Figure 6 shows the proportion of patients in each CCG who received an antibiotic in 2012, with yellow representing the lowest consumption and dark blue showing the highest. However, high consumption is not always synonymous with inappropriate prescribing. Although high consumption might be responsible for resistance, as shown earlier, inappropriate prescribing can be associated with other negative outcomes such as adverse drug reactions (ADRs) and deterioration of patients' clinical outcomes (Levent *et al.* 2012).

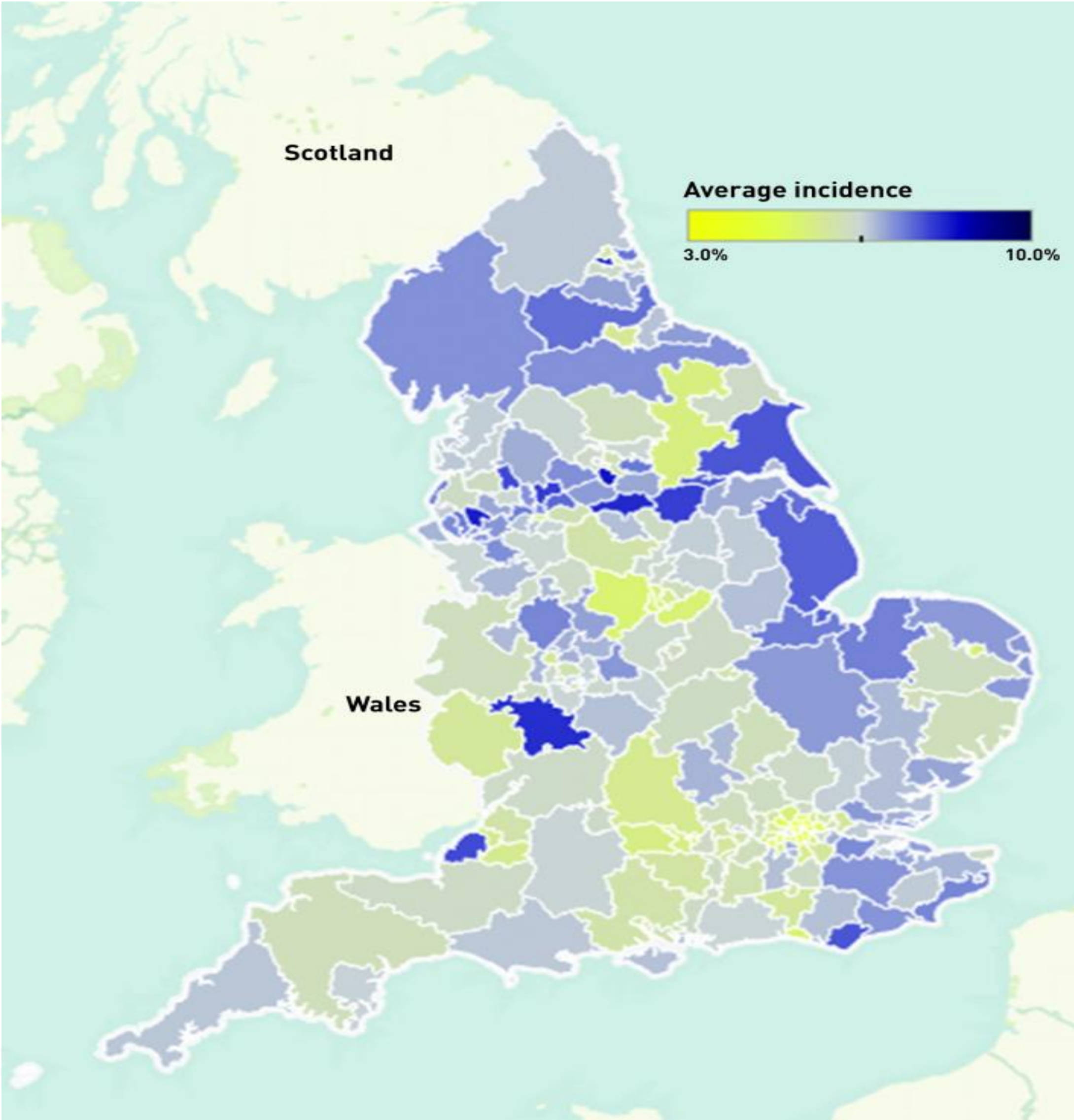



Figure 6: Proportion of registered patients in each CCG who received an antibiotic in 2012 (Shallcross and Davies 2014, p. 604)

## 1.4 Ageing and the Elderly

### 1.4.1 An Ageing and Elderly Population

Ageing by itself is a diverse, inevitable, natural, complex and multi-factorial process in which populations age at different rates and different stages because of both differences in population genetics and the influence of a wide range of environmental factors such as diet, exercise, exposure to pathogens, pollutants and ionising radiation (Nigam *et al.* 2012, Shrivastava *et al.* 2013). The term *'ageing'* does not have a concrete definition that can be generalised to all individuals (Albert and Freedman 2010). However, it is usually measured by chronological age, that is, time elapsed since birth; and any person aged 65 years or over is often referred to as *'elderly'* (Orimo 2006, Shi *et al.* 2008, WHO 2010, Singh and Bajorek 2014). From the age group perspective, people 65 years old are classified as *'old'* or *'older'*, while those from 65 through 74 years old are classified as *'early-elderly'* and those over 75 years old are classified as *'late-elderly'*. However, the evidence on which this definition is based is unknown (Orimo 2006).

Worldwide, there has been a dramatic shift in societies' demographic structures in terms of the ageing phenomenon. Population ageing has become a universal phenomenon with a historic increase of individuals aged 65 by 10 million per year (Kinsella and Velkoff 2002, Lunenfeld 2008). WHO has predicted that, by 2050, the population aged 60 years and over is expected to increase from 900 million in 2015 to 2 billion people, which equates to an increase from 12% to 22% of the total global population. Furthermore, by 2050, the world will have almost 400 million people aged 80 years or older (WHO 2012a).

This change in societies' demography has been driven by declines in population death rates, caused by longevity, as well as declines in population fertility rates in both developed[14] and developing countries, the introduction of immunisation and improved living standards especially in terms of drinking water, food and sewage (Suzman and Beard 2011). This remarkable improvement in population life expectancy over the past century has perhaps come about as part of the shift in diseases being the leading causes of death. At the dawn of the 20th century, it was infectious diseases that most often claimed the lives of the populations. Currently, non-communicable diseases, that is,

[14] These comprise all regions of Europe and North America, Australia, Japan and New Zealand, while developing countries are those not listed under developed countries (UN 2015).

mainly cardiovascular diseases (CVDs), diabetes mellitus (DM) and stroke, more commonly affect adults and the elderly and impose the greatest burden on global healthcare (Suzman and Beard 2011). Consequently, the global trend in the phenomenon of population ageing will have a dramatic impact on public health, healthcare financing and the delivery of healthcare systems throughout the world (Rechel *et al.* 2013).

Although developed countries, those with an effective rate of industrialisation and individual income (UN 2015), have the oldest elderly profile, the majority of older people and the most rapidly ageing populations are in developing countries, which have a slow rate of industrialisation and low per capita income (UN 2015). Between 2010 and 2050, the number of elderly people in developing countries is projected to increase by more than 250%, compared with a 71% increase in developed countries (Suzman and Beard 2011). Moreover, developed countries, which have already shown a dramatic increase in people over 65 years of age, will experience a progressive ageing of the elderly population (Lunenfeld 2008). Figure 7 lists some examples of countries ranked by population age 60 years and over.

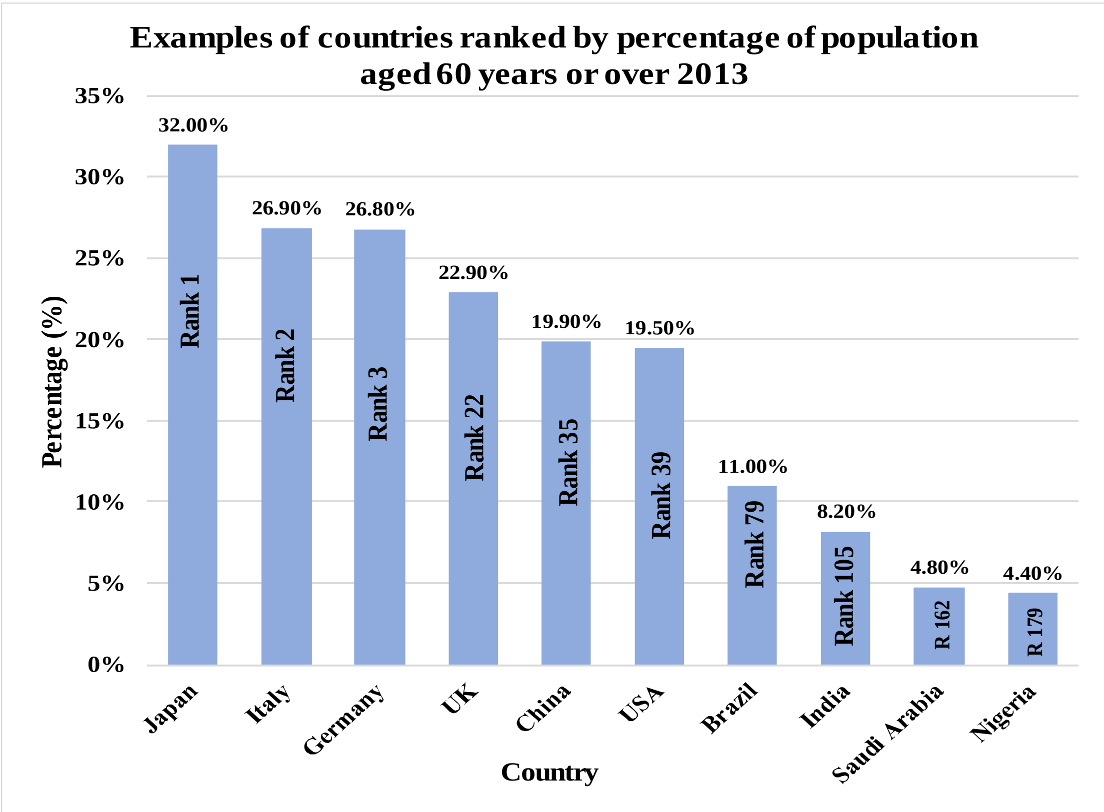



Figure 7: Examples of countries ranked by percentage of population aged 60 years or over, 2013 (UN 2013)

In the UK, the population aged 65 and over has grown by 47% since mid-1974 to make up nearly 18% (N = 11,627,424) of the total UK population in mid-2014. Furthermore, the number of people aged 75 and over has increased by 89% over the same period and now makes up 8% (N = 5,167,744) of the UK population. Compared with mid-2013, the number of older people has grown from 11.1 million (17.4%) in mid-2013 to over 11.6 million (18%) in mid-2014 (ONS 2015b). It has been projected that by 2033 nearly 23% (N = 16,473,290) of the UK population will be over 65 years old compared with 16.4% (N = 9.2 million) in 2011 (Hestbaek *et al.* 2014). Figure 8 compares the percentage of aged population in the UK between 2011 and 2033. Therefore, the coming years will see high demand for healthcare services and resources, particularly for elderly care (Orlu-Gul *et al.* 2014).

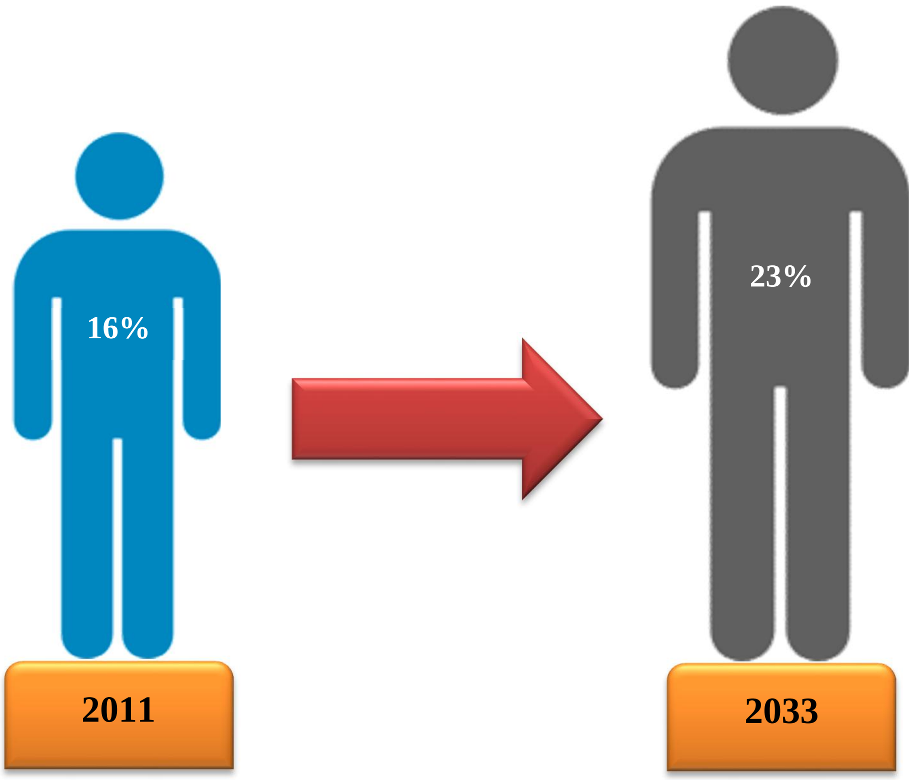



Figure 8: Comparison between the UK population aged 65 in 2011 and the projected elderly population in 2033 (Hestbaek *et al.* 2014)

In the UK, preliminary data from a recently published ONS report revealed that elderly population mortality rates increased in 2015 by 5.4% equating to almost 27,000 extra deaths in just one year (ONS 2016). ONS figures show that mortality numbers have fallen steadily since the 1970s, but the trend began to reverse in 2011 (ONS 2014). This rise in mortality rate has made many health experts call for an urgent investigation into this dramatic increase in elderly mortality.

### 1.4.2 Changes Associated with Ageing

When ageing occurs, the progressive change in physiology starts to affect the whole body, causing a decline in the function of multiple organs and systems such as the central nervous systems (CNS), the cardiovascular system (CVS), the gastrointestinal tract (GIT), the musculoskeletal system and the immune system. However, the magnitude of these changes is hard to estimate (Homeier 2014). As a consequence of this loss from the body's functional reserve, elderly people become more susceptible to triggers to the extent that any weak trigger may result in major morbidity and perhaps mortality (Durso *et al.* 2010). This in part might explain why the prevalence of many diseases usually increases exponentially with advancing age (Shi *et al.* 2008). Hence, ageing is associated with many physiological changes in addition to increased risk of co-morbidity, which can be defined as *'combination of additional diseases beyond an index disorder'* (Marengoni *et al.* 2011, p. 430) or multi-morbidity which can be defined as *'the coexistence of multiple chronic diseases'* (Marengoni *et al.* 2011, p. 430). Therefore normal ageing-related physiological changes must be distinguished from specific diseases that usually develop in old people (Timiras 2007).

Among others, the ageing process affects the urinary system, also known as the renal system. Anatomically, it consists of six organs: two kidneys, two ureters, the urinary bladder and the urethra (Scanlon and Sanders 2011). The system is almost identical in both genders except for a smaller bladder capacity and shorter and straight urethra in females compared to males (Tortora and Derrickson 2008). Additionally, the urethra in males serves not only the urinary system but also the reproductive system, by carrying semen, that is, fluid that contains sperm (van De Graaff 2002). Within the urinary system, the kidneys perform most of the functions compared with the other organs, which act mainly as either passageways or storage areas. The kidneys are responsible for urine formation (McCorry 2004). Other important functions of the kidneys are mainly regulatory in nature and directly related to blood. These functions include regulation of blood pressure, blood pH, blood electrolytes composition, blood volume and blood glucose level; maintenance of blood osmolarity; hormone production; and excretion of waste and foreign substances such as creatinine, urea and ammonia (Scanlon and Sanders 2011).

With advancing age, many anatomical and functional changes can occur in the urinary system. Anatomically, the kidneys can shrink and blood supply can decrease, as can the number of nephrons – the kidneys' functional and structural units – often to half the original number by the age of 70 to 80. This reduction in nephrons can lead to loss of some of the kidneys' concentrating abilities. Other changes in the urinary system may include reduced urinary bladder size and decreased tone of the detrusor muscle, which can lead to frequent urination and poor urine voiding, which can leave a residual volume of urine in the bladder and predispose elderly to infection (Čukuranović and Vlajković 2005, Macias Nuñez *et al.* 2008).

### 1.4.3 Infections in the Elderly

Infections in elderly people compared with younger persons are relatively more frequent, severe and serious as a result of reduced body functional status (Heppner *et al.* 2013). Thus, it should never be underestimated (Norman and Yoshikawa 2009). The elderly are more prone to get colonised and infected with resistant pathogens, which can be associated with increasing treatment failure and risk of complications and eventually contribute to a higher mortality rate since infections are considered a leading cause of death in this age group (Bradley 2007, Beckett *et al.* 2015). Frequently isolated resistant pathogens in elderly people include methicillin-resistant *Staphylococcus aureus* (MRSA), penicillin-resistant *Streptococcus pneumoniae* (PRSP), vancomycin-resistant enterococci (VRE) and multiple-drug-resistant gram-negative bacilli (MDRGNB) (Yoshikawa 2002, Heppner *et al.* 2013). Infections caused by these resistant pathogens are associated with two- to 20-fold higher mortality rates compared with infections caused by antibiotic-susceptible pathogens (Denkinger *et al.* 2013). Figure 9 illustrates the mortality rate in the elderly compared with younger individuals for common infections.

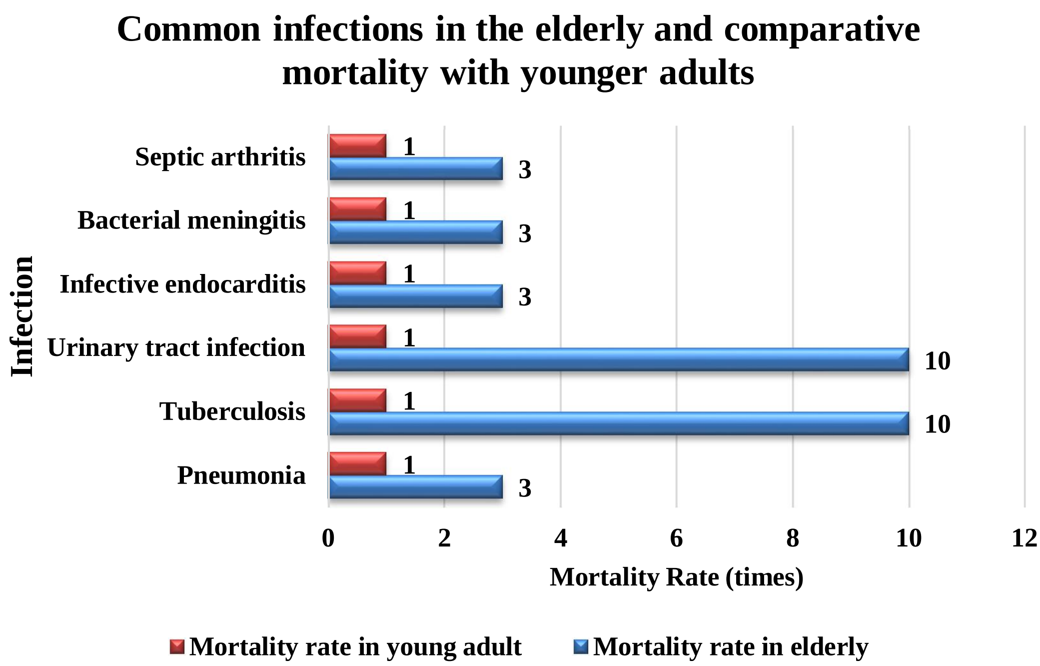



Figure 9: Common infections in the elderly and comparative mortality with younger adults (Norman and Yoshikawa 2009)

Elderly susceptibility to infection was found to be multi-factorial; however, no single factor has been identified as being solely responsible (Adedipe and Lowenstein 2006). The relationships between these risk factors may be very complex (Bradley 2007, Weber *et al.* 2009). These factors include ageing; immune system changes and developing immunosenescence, that is, diminished host defences; presence of underlying co-morbidities such as DM, malignancy and cerebrovascular accidents (CVA); malnutrition; impaired functional status; increased exposure to infections particularly nosocomial infections; complications from diagnostic and therapeutic procedures; and delays in diagnosis and treatment as well as ADRs associated with antibiotics and complications of polypharmacy (Htwe *et al.* 2007, Heppner *et al.* 2013). For example, the elderly have an increased prevalence of UTIs because of age-related anatomic changes in the urinary system, including prostatic enlargement in males, altered physiology and increased bladder residual volume (Htwe *et al.* 2007, Heppner *et al.* 2013).

### 1.4.4 Special Considerations in Antibiotics Prescribing: An Elderly Perspective

Owing to the world population increasingly ageing and the high incidence of infection that might be associated with risk of mortality, it is crucial for all HCPs to ensure that use of antibiotics for suspected infection is appropriate and rational (Herring and Williamson 2007, Weber *et al.* 2009). In England, more than 30% (N = 11,760,000) of the 39.2 million antibiotic prescriptions that were reported in 2007 were dispensed to patients aged 60 years or over (Wang *et al.* 2009). Therefore, GPs must carefully balance antibiotics efficacy, safety and tolerability (Pea 2015) and avoid significant consequences such as ADRs which can be defined as:

> *'A response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function'* (Cluff *et al.* 1972, p. 9),

drug interactions and risks associated with drug-resistant pathogens and *Clostridium difficile* (Beckett *et al.* 2015) whenever there is a need to prescribe an antibiotic for an elderly patient.

In the elderly, several issues should be considered before prescribing an antibiotic. These issues include the patient's multi-morbidities or co-morbidities, poor compliance and impaired mental and functional state, age associated pharmacokinetic (PK) and pharmacodynamic (PD) changes, infected pathogens, as well as polypharmacy with the inherent risk of ADRs and drug–drug interactions (Borrego and Gleckman 1997, Stalam and Kaye 2004, Corsonello *et al.* 2015). Most of the literature about the effects of ageing on antibiotics is relatively new (Herring and Williamson 2007) and the use of antibiotics in elderly patients has been found to bring numerous challenges (Beckett *et al.* 2015). This could be owing to the elderly population were excluded from clinical trials of old antibiotics and underrepresented in clinical trials of recent ones (Beckett *et al.* 2015). Therefore, it is important to understand the relationship between ageing and antibiotics to avoid any risk or form of inappropriate prescribing in this vulnerable age group.

#### 1.4.4.1 Antibiotics and Age-related PK and PD Changes

Several age-related physiological changes can influence and alter the four main components of PKs, that is, what the body does to the antibiotic, namely, absorption, distribution, metabolism and excretion (Weber *et al.* 2009, Asin-Prieto *et al.* 2015). PK changes must be considered when treating infection in elderly patients as understanding these could lead to significant improvement in the quality and appropriateness of antibiotics prescribing in relation to choice, dose, frequency and route of administration (Bergman *et al.* 2007). Ageing can affect PD, which include the pharmacological effects of antibiotics on receptors, tissues and organs. These changes may alter the number of receptors and affinity, signal transduction and homeostatic mechanisms. The effects may result in greater therapeutic benefits as well as increased potential for antibiotic toxicity and sensitivity (Aymanns *et al.* 2010). Table 5 summarises and provides examples of the common changes in PK components and PD in the elderly and the influence of these changes on antibiotics.

Table 5: PK and PD issues to consider when prescribing antibiotics for elderly patients(Herring and Williamson 2007, Bellmann-Weiler and Weiss 2009)

| | Implications | Age-related change | Effect | Example |
|---|---|---|---|---|
| **PK** | **Absorption** | ↓ gastric acidity | ↓ absorption | Cefuroxime<br>Sulphonamides |
| | | | ↑ absorption | Erythromycins<br>Clarithromycin<br>Penicillins |
| | | ↓ gastric emptying | ↓ peak concentrations | Ciprofloxacin in diabetic patient with gastroparesis |
| | | ↓ surface area of intestinal mucosa and reduced blood flow | Influence the rate and extent of absorption | Macrolides<br>Quinolones<br>Cephalosporins (3rd generation) |
| | **Distribution** | ↑ in adipose tissues and reduced total body water | ↑ Vd and prolongation of $t_{½}$ lipid-soluble antibiotic | Fluoroquinolones<br>Macrolides<br>Clindamycin<br>Tigecycline |
| | | | ↓ Vd and high serum level of water-soluble antibiotic | Beta-lactams<br>Aminoglycosides<br>Vancomycin<br>Linezolid |
| | **Protein binding** | displacement of antibiotic protein binding site by other molecule such as uric acid, bilirubin or other high protein binding medication | ↑ free concentrations of acidic antibiotic | Sulphonamides<br>Penicillins<br>Doxycycline<br>Cephalosporins<br>Nitrofurantoin |
| | | ↑ α1-acid glycoprotein | ↓ free concentration of basic antibiotic | Macrolides |
| | **Clearance** | ↓ liver blood flow | Slower rate of clearance | Quinolones<br>Macrolides |
| | | ↓ renal blood flow | Slower rate of renal excretion | Aminoglycosides<br>Beta-lactams<br>Glycopeptides |
| | **Metabolism** | ↓ liver blood flow and mass | ↑ oral bioavailability due to reduced first pass metabolism | Clarithromycin |
| | **Excretion** | ↓ renal blood flow and GFR | ↑ $t_{½}$ of renal eliminated antibiotic | Aminoglycosides<br>Beta-lactams<br>Glycopeptides |
| **PD** | **Toxicity/ADRs** | ↑ sensitivity | Hypoglycemia | Gatifloxacin |
| | | | Confusion, seizures<br>Psychoses | Levofloxacin<br>Moxifloxacin |
| | | | QT interval prolongation | Moxifloxacin |

Vd: Volume of distribution; $t_{½}$: half-life; GFR: glomerular filtration rate; ↓: decreased; ↑: increased

### 1.4.4.2 ADRs Associated with Antibiotics in the Elderly

It is well documented that with advancing age, the risk, frequency and severity of developing ADRs are increased (Norrby 1987, Herring and Williamson 2007). Although elderly individuals have a two- or three-fold higher chance of developing ADRs from antibiotics compared with younger age groups (Routledge *et al.* 2004, Bellmann-Weiler and Weiss 2009), age by itself has not been identified as a consistent independent risk factor for ADRs in elderly patients. Other risk factors may include multi-morbidities or co-morbidities, disease severity, host sensitisation owing to previous administration of antibiotics, metabolic conversion, increased drug deposition in the body, impaired renal function, administration of unnecessarily large doses of antibiotics for long periods, concomitant drugs use or concurrent therapy administered simultaneously with antibiotics, poor compliance and age-related PK and PD changes (Faulkner *et al.* 2005, Herring and Williamson 2007).

In the UK, one systematic review showed that antibiotics were one of the six classes of drugs responsible for 60%–70% of all ADR hospital admissions in elderly patients (Wiffen *et al.* 2002). Two prospective European studies showed that administration of antibiotics in the elderly may result in emergency department visit and hospital admission (Olivier *et al.* 2009, Conforti *et al.* 2012). ADRs associated with antibiotics in the elderly can range from simple GIT manifestations such as nausea, vomiting and diarrhoea to more serious ADRs such as arrhythmia and bone marrow suppression (Bolon and Weber 2009). Table 6 lists some of the commonly used antibiotics and the associated ADRs that can occur in elderly patients.

Table 6: Examples of ADRs of commonly used antibiotics in the elderly for UTIs(Bolon and Weber 2009, p. 1522)

| Antibiotic class/drug | Common ADRs |
|---|---|
| Beta-lactam agents | Rash, hypersensitivity reactions, bone marrow toxicity, CNS toxicity (seizure), interstitial nephritis, antibiotic-associated diarrhoea, *Clostridium difficile*-associated diarrhoea |
| Fluoroquinolones | QT prolongation, torsade de pointes, CNS toxicity, peripheral neuropathy, tendon rupture, *Clostridium difficile*-associated diarrhoea |
| Nitrofurantoin | Pulmonary infiltrates, peripheral neuropathy |
| Sulphonamides | Rash, hypersensitivity, Stevens-Johnson syndrome, GIT toxicity (nausea, vomiting), hyperkalaemia, bone marrow suppression |

### 1.4.4.3 Antibiotics and Polypharmacy

In elderly patients, concomitant administration of multiple drugs, that is, polypharmacy, is often the rule rather than the exception (Mangoni 2012, Corsonello *et al.* 2015). Definitions of polypharmacy in the elderly vary greatly across the literature. In the European literature, researchers defined polypharmacy quantitatively according to the number of drugs administered; whereas in the American literature researchers used qualitative measures to define polypharmacy such as whether the administered drug was clinically indicated or not (Fulton and Allen 2005). Some literature defined polypharmacy as concurrently taking two or more drugs for 240 days or more (Veehof *et al.* 2000). Other literature arbitrarily defined polypharmacy as administering two to nine drugs concurrently (Bjerrum 1999, Bikowski *et al.* 2001, Jorgensen *et al.* 2001, Linjakumpu *et al.* 2002, Fulton and Allen 2005). Other definitions based on qualitative measures include the prescription, administration or use of more drugs than are clinically indicated in a given patient (Montamat and Cusack 1992) or untoward iatrogenic sequela caused by the use of multiple, interacting drugs (Fillit *et al.* 1999). In the UK, 80% of people aged 75 years or over were prescribed at least one drug and more than 66% are prescribed four or more medications (Fitzgerald and Pirmohamed 2007).

Polypharmacy in the elderly has been recognised as being associated with negative outcomes such as risk of developing serious drug–drug interactions (Shah and Hajjar 2012, Maher *et al.* 2014). However, these interactions can be predictable and avoidable (Mangoni 2012, Corsonello *et al.* 2015). Antibiotics may interact with other drugs in different ways, including displacing a drug from plasma protein binding sites, interacting with liver enzymes and competing for tubular secretion in the kidney (Biedron and Chopra 2013). An example of common drug–drug interaction resulted from polypharmacy in elderly patients using antibiotics is trimethoprim-sulfamethoxazole (TMP-SMX) with warfarin, which can cause severe elevation in the international normalisation ratio (INR) and bleeding or TMP-SMX with spironolactone, resulting in elevation of the blood potassium level (hyperkalaemia), which in turn can lead to hospitalisation and expose elderly patient to sudden death (Wei *et al.* 2011, Fralick *et al.* 2014). Therefore, GPs must be careful while prescribing antibiotics to ensure that the resulting polypharmacy does not expose the elderly patient to negative consequences (Wallace and Paauw 2015). Table 7 lists some of the antibiotics commonly used in the elderly along with examples of the drug–drug interactions that can occur.

Table 7: Common drug–drug interactions involving antibiotics prescribed to elderly patients for UTIs (Nicolle 2009a)

| Antibiotic class/drug | Interacting drugs | ADRs |
|---|---|---|
| Cephalosporins | Aminoglycosides | ↑ Nephrotoxicity |
| | Furosemide | ↑ Nephrotoxicity |
| TMP-SMX | ACE-I/ARBs | ↑ Risk of sudden death due to hyperkalaemia |
| | Spironolactone | ↑ Risk of sudden death due to hyperkalaemia |
| Nitrofurantoin | Antacids | Possible ↓ nitrofurantoin effect |
| | Fluoroquinolones | In vitro antagonism of quinolone activity |
| Fluoroquinolones | Antacids | ↓ Floroquinolone effect |
| | Oral anticoagulants | Prolonged prothrombin times |
| | Cyclosporine | ↑ Risk of nephrotoxicity; increased serum cyclosporine concentrations |
| | Iron | ↓ Serum fluoroquinolone concentrations |
| | NSAIDs | Possible ↑ risk of CNS stimulation |
| | Sucralfate | ↓ Serum fluoroquinolone concentrations |

NSAIDs. Nonsteroidal Anti-Inflammatory Drugs; ACE-I: Angiotensin-Converting Enzyme Inhibitors; ARBs: Angiotensin II Receptor Blockers; ↓: decreased; ↑: increased

### 1.4.4.4 Appropriate Antibiotics Prescribing in the Elderly

Given the issues applicable to elderly patients, a somewhat modified approach is needed for treating their infections appropriately from that followed traditionally for the rest of the population (Stalam and Kaye 2004, Herring and Williamson 2007). That said, the general principles for the treatment of infection are relatively the same. These include early and rapid diagnosis of infection then rapid initiation of broad empirical therapy with appropriate microbial coverage of the suspected pathogens followed by the narrowing or discontinuation of an antibiotic based on the patient's clinical status and on pathogen identification following the culture result (Herring and Williamson 2007, Bolon and Weber 2009, Rho 2009). However, this can be challenging with elderly patients because they lack many classic signs and symptoms of infection, which can be further hindered by mental and cognitive impairment and specific complaints from multi-morbidities or co-morbidities in addition to infection with more diverse and resistant bacteria (Norman and Yoshikawa 2009). Thus, the process of early and rapid detection and diagnosis of infection and early initiation of antibiotic therapy can be delayed (Yoshikawa 2000). Table 8 lists the principles for optimising and promoting appropriate antibiotics prescribing in elderly patients.

Table 8: General guiding principles for optimising and promoting appropriate antibiotic prescribing in elderly patients (Herring and Williamson 2007, p. 482)

- Risk stratify patients for severe infections and multidrug-resistant pathogens based on lifestyle and functional status
- Provide early and broad empiric therapy using national guidelines and local resistance patterns when available
- Obtain a complete medication history and carefully select antibiotics to avoid severe drug-drug interactions and drug-disease interactions
- Dosing of antibacterial should consider age-related changes in PK and PD parameters, but maximal therapeutic dosing should not be sacrificed to avoid potential ADRs
- De-escalate antibiotic therapy based on the patient's clinical status and identified pathogen
- Consider participation in studies of antibiotics in elderly populations and report adverse drug events when they occur to augment clinical information
- Dose reduction may be needed due to decreased lean body mass of the elderly especially older females
- Dose intervals for renally excreted antibiotics may need to be lengthened because of reduced renal function
- Conservative, full-course therapy is usually preferred for all infections
- Oral therapy offers more convenience, and avoided antibiotics with a narrow therapeutic window such as aminoglycosides and vancomycin when possible

Antibiotics choice for elderly patients should be based on identification of the infection site and severity and the possible causative pathogen, antibiotics efficacy, the patient's renal and hepatic function, dosage and route of administration, local AMR patterns, and the unique PK and PD features of the antibiotic as well as the potential ADRs and drug interactions (Bolon and Weber 2009, Rho 2009, Beckett *et al.* 2015). A careful and comprehensive history and examination of the patient, as well as careful collection of an appropriate sample, are prerequisites for any antibiotics prescription. Initially, antibiotic therapy is empiric, requiring consideration of the most causative pathogen in a given infection. The choice of empirical antibiotic regimen should be based on the disease severity, the nature of any underlying diseases and multi-morbidities or co-morbidities, prior exposures to antibiotics and history of antibiotic allergies. Once empiric therapy is initiated, the patient's clinical progress needs to be closely followed and the antibiotic regimen broadened or narrowed according to the results of the culture and sensitivity tests (Bolon and Weber 2009, Rho 2009, Beckett *et al.* 2015).

## 1.5 UTIs in the Elderly

### 1.5.1 Definition of UTIs

A UTI can be defined as:

> *'The presence and multiplication of microorganism(s), in one or more structures of the urinary tract, with associated tissue invasion'*(Cowling *et al.* 2014, p. 8).

The term UTI is broad and includes a wide range of clinical syndromes that differ from each other in infection severity and site (Lane and Takhar 2011). UTIs can range from relatively simple, easy-to-treat infections such as cystitis (infection in the bladder), urethritis (infection in the urethra), epididymitis (infection in the epididymis of the testicles) and prostatitis (infection in the prostate gland) to more complex, difficult-to-treat infections such as pyelonephritis (infection involving the kidneys and the renal pelvis) (Cowling *et al.* 2014, Rudolf *et al.* 2015). Figure 10 demonstrates the sites for different types of UTI.

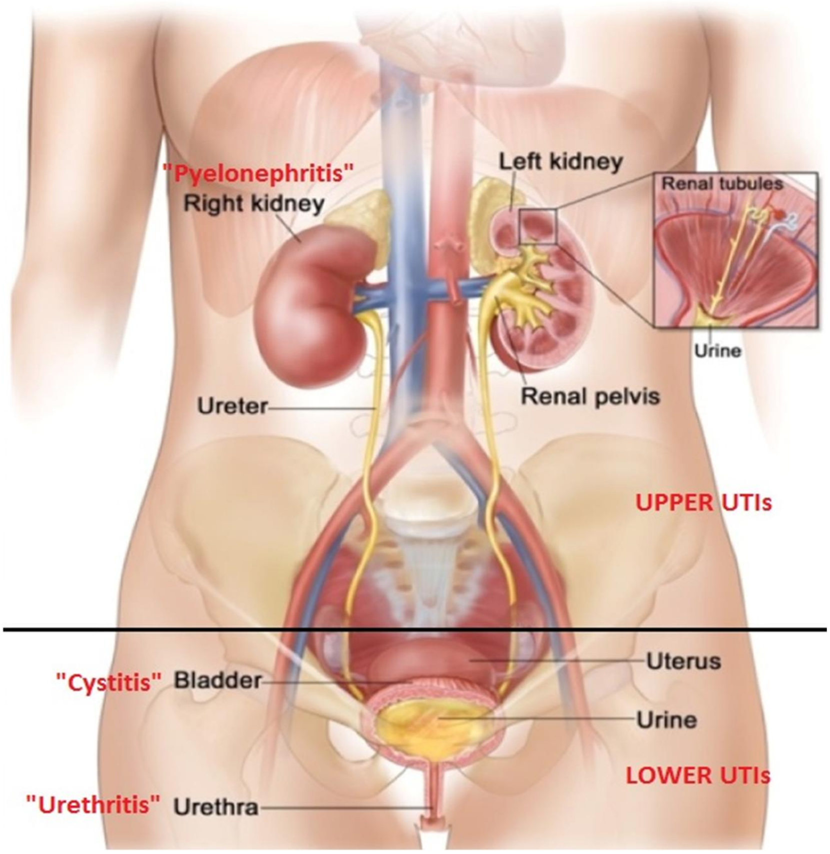



Figure 10: Anatomy of the female urinary tract system with classification of UTIs (Winslow 2010)

UTIs may spread to the tissue surrounding the kidneys, causing scarring that in turn can lead to end-stage renal diseases (McGladdery *et al.* 1992, Cullen *et al.* 2013), to perinephric abscess (Neumann *et al.* 2005, Rudolf *et al.* 2015) or to the bloodstream, causing sepsis and death (Tal *et al.* 2005). In the UK, a retrospective clinical and laboratory data analysis of 104 patients showed that more than one-quarter (N = 17) of elderly patients aged over 70 later diagnosed as having bacteremic UTI initially presented with confusion and fall (Barkham *et al.* 1996). Despite there being several available guidelines (Gupta *et al.* 2011) with different aims that have been developed by various related interest groups in recent years, a universally accepted and concise definition of UTIs and their associated symptoms in the elderly population does not exist (Rowe and Juthani-Mehta 2014, Detweiler *et al.* 2015).

### 1.5.2 Classification of UTIs

Over the past 20 years, many classification systems have been proposed to sub-classify different types of UTI. Distinctions between the different UTI classes can be important for selecting the appropriate antibiotic drug, duration of therapy, quality measurement and for research and teaching purposes (Johansen *et al.* 2011).

UTIs are frequently classified according to location of infection, presence or absence of signs and symptoms, presence or absence of complicating factors and frequency of infection (Nelson and Good 2015). The most widely used UTI classification systems are those established by the Centre for Disease Control and Prevention (CDC) (Garner *et al.* 1988), updated in 2008 (Horan *et al.* 2008); the Infectious Diseases Society of America (IDSA) (Rubin *et al.* 1992); the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) (Rubin *et al.* 1992); and the European Association of Urology (EAU)/European Section for Infections in Urology (ESIU) (Grabe *et al.* 2010), updated in 2015 (Grabe *et al.* 2015). Table 9 summarises the different UTI classes according to site, signs and symptoms, recurrence and completed co-morbidities, and predisposing factors using laboratory findings from midstream urine (MSU) samples obtained from patients and including both the number of infecting microorganisms (expressed in colony-forming units (cfu)) and the number of white blood cells (WBCs) within the urine samples. The table was generated as an attempt to collect all the different types of UTI into one table based on the different classifications.

Table 9: Classifications and definitions of UTIs according to site, signs and symptoms, recurrence and completed co-morbidities and predisposing factors (SIGN 2012, McNulty *et al.* 2014, Grabe *et al.* 2015)

| Term | Types | Definition | Laboratory investigations | Special considerations in elderly |
|---|---|---|---|---|
| **Anatomic** | **Upper** | Pyelonephritis is a clinical syndrome characterised by inflammatory process of the renal pelvis, renal parenchyma and ureters due to an infection. It can be either acute or chronic (recurrent). Symptoms may include loin pain, flank tenderness, fever, rigors | > 10 WBC/$mm^3$<br>> $10^4$ cfu/mL uropathogen in MSU culture | |
| | **Lower** | Infection confined to the tissues of the bladder (cystitis) or urethra (urethritis)<br>Cystitis is a clinical syndrome characterised by inflammatory process of the bladder which associated with dysuria or frequency without fever, chills or back pain<br>Prostatitis (prostate gland): inflammatory condition of the prostate gland that occurs in a variety of different forms | > 10 WBC/$mm^3$<br>> $10^3$ cfu/mL uropathogen in MSU culture | |
| **Symptoms** | **Symptomatic UTIs** | Presence of bacteriuria in urine revealed by quantitative culture or microscopy in a sample taken from a patient, or the typical symptoms of lower or upper UTI. The presence of symptomatic bacteriuria can be established with a single urine sample | | |
| | **ASB** | Presence of bacteriuria in urine revealed by quantitative culture or microscopy in a sample taken from a patient without any typical symptoms of lower or upper UTIs. Asymptomatic bacteriuria should be confirmed by two consecutive urine samples | > 10 WBC/$mm^3$<br>> $10^5$ cfu/mL uropathogen in MSU culture in two consecutive MSU cultures > 24 hour apart | ≥10 WBC/$mm^3$ of uncentrifuged urine in women is not enough to diagnose a UTI in men rare to have contaminated urine samples |
| | **Recurrent** | The occurrence of ≥ 3 UTIs within a 12-month period or ≥ 2 UTIs within a 6-month period. Recurrence can be either relapse which can be defined as persistent infection with the same pathogen isolated before the therapy, despite adequate therapy, or reinfection which can be defined as isolation of a pathogen which may be either a new bacterial strain or a previously isolated strain that has colonised another area of the urinary tract | < $10^3$ cfu/mL uropathogen in MSU culture | Need to distinguish between relapse and reinfection |
| **Complexity** | **Uncomplicated** | Infection in a structurally, functionally, and neurologically normal urinary tract | $10^5$ cfu/mL uropathogen in MSU culture<br>Culture may be omitted if patient is symptomatic and dipstick is + for leukocyte esterase and nitrites | Check for negative culture after therapy to prevent partial treatment or resistance |
| | **Complicated** | Infection in urinary tract due to the presence of factors that predispose to persistent or relapsing infection, such as medical condition, co-morbidities or predisposing factors that interfere with normal flow of urine or voiding mechanism | > 10 WBC/$mm^3$<br>> $10^5$ cfu/mL uropathogen in MSU culture in women<br>> $10^4$ cfu/mL uropathogen in MSU culture in men, or in straight catheter urine in women | Have low-threshold for imaging studies or cystoscopy to rule out urinary stasis and/or stones |

ASB: Asymptomatic Bacteriuria, CFU: Colony-Forming Units, WBC: White Blood Cells, MSU: Midstream Urine

### 1.5.3 Burden and Epidemiology of UTIs in the Elderly Population

UTIs were found to pose a huge burden on both patients and healthcare funding systems, being common and costly (Keating *et al.* 2005). A survey conducted in the USA estimated the total cost of UTI illness to be $1.6 billion in 1995 and was projected it to be $2.8 billion in 2014 (Foxman *et al.* 2000). The global incidence of UTIs was estimated to be at least 250 million cases annually (Ronald *et al.* 2001). According to NICE, UTIs account for 1%–3% of all general practice consultations per annum in the UK (NICE 2015b). Furthermore, a HSCIC report based on NHS England statistical data for 2012–2013 demonstrated that UTIs were one of the most frequent reasons for emergency hospital admissions, despite NHS England indicators (NHSOF 3a) showing conditions that should be managed without patients having to be admitted. The report showed that UTIs resulted in 67 admissions per 100,000 population, per quarter, on average for 2012–2013 (HSCIC 2014a). Further, a medical database analysis of 179 GP surgeries in the UK showed that UTIs were responsible for 7% (N = 89,795) of all infectious disease consultations in 1990–2001 (Petersen and Hayward 2007a, Petersen and hayward 2007b).

Worldwide, almost 10% of elderly people get infected with UTIs (Kelly-Fatemi 2015). In primary care, UTIs comprise the second most common type of infection in the elderly after respiratory tract infections (RTIs) (Robichaud and Blondeau 2008, Matthews and Lancaster 2011) and are ranked the second most common cause of infectious disease hospitalisation in the elderly after lower RTIs according to a study of the Discharge Survey database from 1 January 1990 through 31 December 2002 (Curns *et al.* 2005). In the UK, it was reported that UTIs in the elderly resulted in over 150 consultations per 1,000 patients in 2000 alone (Petersen and Hayward 2007a, Petersen and hayward 2007b). Figure 11 shows the UK general practice consultations for UTIs among all age groups including the elderly from 1991 to 2000. In 2010, UTIs were reported as cause number 19 of death in the UK for patients older than 70, after they were cause number 41 in 1990 (IHME 2010). Since estimation of the prevalence[15] of UTIs in elderly patients in the UK is one of this thesis' main objectives, the epidemiology of UTIs in elderly populations is discussed in more detail in Chapter Two.

[15] Measures of all cases in the population who have the disease within a specified time frame (Kier 2011, p. 12).

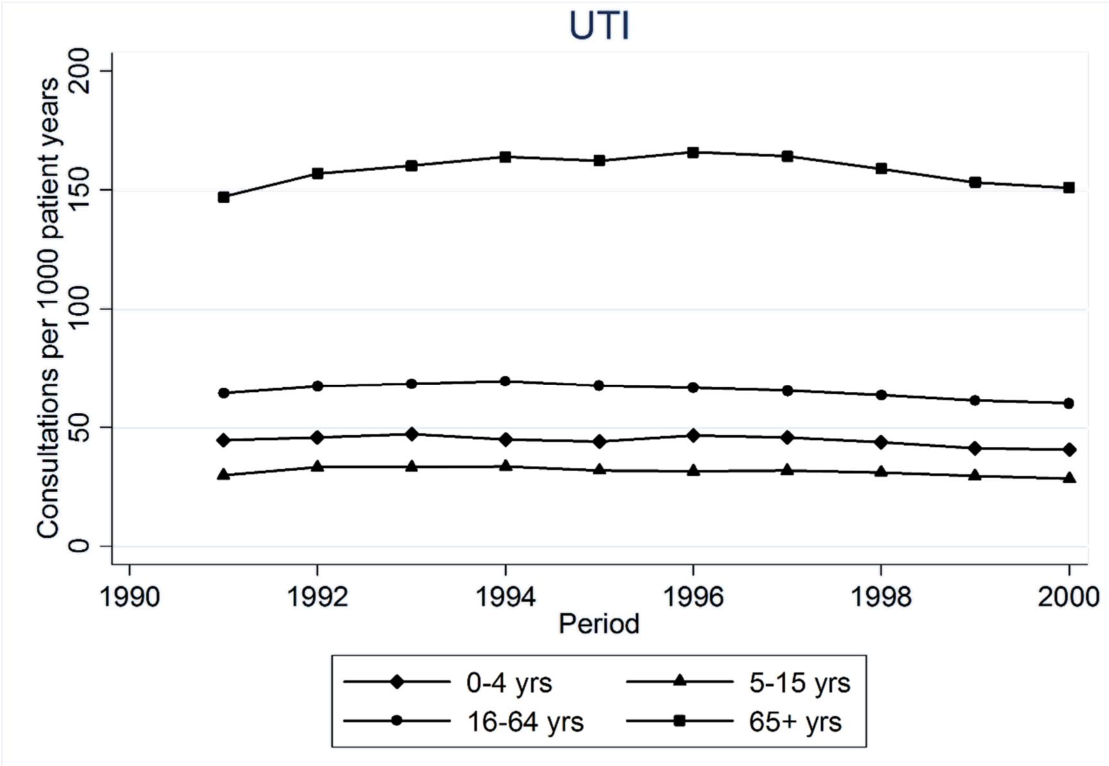



Figure 11: UTI general practice consultations per age group in the UK between 1991 and 2000 (Petersen and Hayward 2007a, Petersen and hayward 2007b)

### 1.5.4 Pathophysiology and Risk Factors of UTIs in the Elderly

Normally, urine is a sterile fluid, but in some conditions it might become a good medium for bacterial growth when bacteria invade and colonise the urinary bladder (McCorry 2004). In UTIs, bacteria can reach the urinary tract system and cause infection by two major routes. The first, the ascending route, is the most common, whereby bacteria from the GIT flora usually colonise the periurethral region before penetrating and colonising the urinary tract through the urethral opening. The second route is haematogenous seeding of the kidney during bacteraemia (Nelson and Good 2015).

Numerous factors may contribute to the high frequency of UTIs in elderly populations, although they are not all fully understood. Factors related to genetics, gender, anatomy and age-associated changes in immunity are considered to be responsible for UTIs in elderly patients (Beveridge *et al.* 2011); whereas disability in daily living, cognitive impairment, urinary incontinence and prior or recent UTI history are considered to be the strongest predictors of UTI risk (Hu *et al.* 2004, Foxman 2014). In post-menopausal females, the lack of oestrogen has been linked with UTI recurrence (Perrotta *et al.* 2008). The change in post-menopausal females' vaginal flora in which the lactobacilli that maintain the vaginal pH are replaced by *Escherichia coli (E. coli)* and the enterococcus species is another predisposing factor for UTIs in elderly people (Nicolle 2009b). Sexual activity has also been found to increase the risk of UTIs in elderly females; although these findings are not as strong as in pre-menopausal females (Moore *et al.* 2008).

Additionally, the presence of co-morbidities such as DM with poor glycaemic control can also increase the risk of developing UTIs (Ronald and Ludwig 2001). Cerebrovascular diseases or neurologic abnormalities can cause impaired bladder voiding, urinary retention and urinary incontinence, which might require insertion of a catheter (Nicolle 2002). Use of urine-collection devices or catheters may allow bacteria to migrate to the bladder, which may result in UTIs (Matthews and Lancaster 2011).

Furthermore, there is a strong association between the presence of certain urologic conditions or abnormalities and increased frequency of UTIs. For instance, conditions such as urolithiasis or tumour are associated with urine flow obstruction (Beveridge *et al.* 2011) and conditions such as cystocele, which increase post-void residual volumes in females, can increase the risk of UTIs (Raz 2011). In males, prostatic diseases such as benign prostatic hypertrophy are associated with urinary retention and high post-void residuals may be associated with developing UTIs (Nicolle 2009c). Table 10 gives examples of risk factors that can increase the chance of UTIs in elderly patients.

Table 10: Factors increasing the risk of UTIs and complexity in the elderly (Wilson and Markland 2014, Sobel and Kaye 2015)

| Factor | Factors for increased UTIs | Factors for complicated UTIs |
|---|---|---|
| ***Urological*** | ***Renal factors:***<br>Previous UTI<br>Urologic instrumentation<br>Urological surgery<br>Urethral catheterisation<br>Obstructive uropathy<br>Nephrolithiasis<br>Calculi<br>Neurogenic bladder<br>Renal transplantation<br>Prostatic enlargement<br>Condom catheter drainage<br>Bladder prolapse<br>Chemical or radiation injury of uroepithelium<br>Dysfunction of the urinary tract | ***Anatomical/ structural abnormalities:***<br>Urethral stricture<br>Ureteric stricture<br>Bladder diverticulum fistulae<br>Urinary diversion<br>Polycystic kidney disease<br>Medullary sponge kidney<br>Diverticula (e.g. calyceal, bladder, urethral)<br>***Foreign body:***<br>Indwelling catheter<br>Ureteric stents<br>Nephrostomy tube<br>Urolithiasis<br>***Functional:***<br>Neurogenic bladder<br>Bladder outflow obstruction (e.g. Benign prostatic hypertrophy, stenosis, ureteral or urethral obstruction)<br>Vesicoureteric reflux<br>***Others:***<br>Urinary tract surgery or instrumentation<br>Renal transplantation<br>Renal malignancy<br>Previous history of acute pyelonephritis in the past year<br>UTIs symptoms for at last 7 days before seeking care<br>Multidrug-resistant pathogen<br>Renal failure<br>History of UTIs in childhood<br>Bladder prolapse |
| ***Non-urological*** | ***General:***<br>Female gender<br>Lack of circumcision (M)<br>Functional or mental impairment<br>Oestrogen deficiency<br>DM<br>Co-morbidities<br>Immunosuppression immunodeficiency<br>Host response capacity<br>Nonsecretor status (F)<br>ABO blood-group antigens<br>Behavioural sexual intercourse<br>Previous use of antibiotics<br>Long hospital stay | ***General:***<br>Male gender<br>Immunosuppression<br>DM<br>Renal insufficiency<br>Nosocomial infection<br>Functional or mental impairment<br>Oestrogen deficiency |

F: Female, M: Male; DM: Diabetes Mellitus

### 1.5.5 Diagnosis

#### 1.5.5.1 Clinical presentations

The gold standard for UTI diagnosis is the presence of clinical symptoms and detection of bacteria in a urine sample (SIGN 2012, McNulty 2015). Clinical presentations of UTIs in the elderly have been well described in much of the literature in relation to polyuria, frequency, urgency, dysuria, new-onset or worsening incontinence, suprapubic pain or tenderness, flank pain and fever greater than 38° Celsius (Juthani-Mehta 2009, Woodford and George 2011). Different types of UTI can vary markedly in terms of clinical symptoms (Sobel and Kaye 2015).

In the UK, PHE and the British Infection Association (BIA) recommend diagnosis of UTIs when at least three of the following symptoms are present: polyuria, frequency, urgency, dysuria, suprapubic tenderness and haematuria (McNulty 2015). However, this is not the case with elderly patients. Diagnosis of UTIs in elderly people can be challenging for HCPs (Ninan *et al.* 2014) as they often present to GP surgeries with atypical disease symptoms that are non-specific to infection such as nausea, vomiting, dehydration, increased weakness, lethargy, change in mental status and confusion, all of which are very common in this age group (Jaff and Paganini 1989, Cohen *et al.* 2011, Nicolle 2013). Moreover, the presence of multiple co-morbidities such as cognitive impairment in addition to limited communication abilities and poor baseline function can make it difficult to obtain an accurate history from the patient (Matthews and Lancaster 2011). The presence of classical UTI symptoms in elderly patients is often not diagnostic because elderly people have other chronic genitourinary symptoms and it is important to recognise that these are not synonymous with UTIs (Stamm and Raz 1999). Furthermore, some or all of these symptoms may be absent in elderly patients despite how serious UTIs are (Jaff and Paganini 1989, Cohen *et al.* 2011, Nicolle 2013). The Scottish Intercollegiate Guidelines Network (SIGN) thus recognises all of these challenges in diagnosing elderly patients with suspected UTIs and recommends full clinical assessment, including vital signs, for all patients aged over 65 (SIGN 2012).

#### 1.5.5.2 Laboratory Evaluation

The wide varieties of potentially infecting pathogens and the increased likelihood of AMR in elderly people have made urine culture testing a gold standard in UTI diagnosis

(SIGN 2012, McNulty 2015). A urine specimen for culture is essential to confirm the diagnosis, identify the specific infecting pathogen and determine the pathogen's susceptibilities to antibiotics (Cowling *et al.* 2014). The PHE guideline states that urine should only be sent for culture if the patient has two or more symptoms of infection, especially fever, dysuria or new incontinence (McNulty *et al.* 2014). A definitive UTI diagnosis requires isolation of appropriate quantitative counts of bacteria from an optimally collected urine specimen before initiating antibiotic therapy in an elderly patient with suspected UTI (SIGN 2012).

Urine specimen must be collected in a way that minimises sample contamination (SIGN 2012). The UK Standards for Microbiology Investigations recommend the MSU clean-catch technique for culturing purpose (Cowling *et al.* 2014). A voided clean-catch urine specimen can be obtained from most elderly patients with suspected UTI. If the patient is confused, incontinent or uncooperative, a specimen can be collected by using an in-and-out catheter in females or an external condom catheter after applying a clean condom and leg bag in males (Genao and Buhr 2012). If the elderly patient already uses a catheter, a new catheter must be used to collect a fresh urine sample for culture (Nicolle 2014). That said, adherence to these standards is lacking in many practices (Pallin *et al.* 2014).

Urinalysis (UA) is a relatively simple, easy-to-use, office-based test to evaluate patients with urinary manifestations (Gibson and Toscano 2012). The urine dipstick tests that are usually used for UA to detect the presence of nitrites and leucocyte esterase are often used as surrogate markers of an elevated urinary pyuria and gram-negative bacteriuria, respectively (Ninan *et al.* 2014). However, the presence of pyuria or bacteriuria does not necessarily mean that the person has a UTI (Woodford and George 2011). A urine dipstick is of limited value for diagnosing elderly patients with suspected UTIs. The SIGN guidelines instruct practitioners against using this test for elderly patients owing to the variations in its accuracy for predicting infection, with nitrites having the highest specificity with poor sensitivity (SIGN 2012).

### 1.5.6 Microbiology of UTIs in the Elderly

The majority of elderly UTI cases in primary care are the result of infection by a single form of bacteria (Wang *et al.* 2013). Greater varieties of pathogens are isolated from elderly persons with UTIs when compared with younger age groups. The most commonly isolated bacterium accounting for 60%-75% of UTI cases in elderly females and 18%–50% of UTI cases in elderly males is gram-negative *E. coli* (Yoshikawa and Rajagopalan 2006, Nicolle 2009b, Nicolle 2009a). Table 11 lists common bacteria isolated from the community and responsible for UTI in the elderly population.

Table 11: Distributions of UTI bacteria isolated from elderly patients in the community (Yoshikawa and Rajagopalan 2006, Nicolle 2009b, Nicolle 2009a)

| **Bacteria** | **Percentage of isolation (%)** | |
|---|---|---|
| | ***Female*** | ***Male*** |
| *E. coli* | 60-75 | 18-50 |
| *Klebsiella pneumoniae* | 7-21 | 0.6-6.9 |
| *Proteus mirabilis* | 0.8-11 | 0.6-19 |
| *Enterobacter species* | 3.5 | 1.7-25 |
| *Providencia species* | - | 1 |
| *Pseudomonas aeruginosa* | 2 | 7-19 |
| *Morganell morganii* | - | 0.7 |
| Coagulase-negative staphylococci | 5.6 | 8.9–53 |
| Group B streptococci | 3-10 | 9.6 |
| *Staphylococcus aureus* | - | 5 |
| Others | - | 5-20 |

### 1.5.7 Antibiotics for UTI Therapy in the Elderly

Antibiotic therapy for UTIs in elderly patients should be based on the most frequent causative bacteria, spectrum of antibiotic activity, efficacy, safety, local and national AMR patterns, tolerability and cost to provide clinically appropriate and cost-effective therapy and to reduce therapy failure and the emergence of bacterial-drug-resistant strains (Gupta *et al.* 1999, Dromigny *et al.* 2002, Bellmann-Weiler and Weiss 2009). Oral antibiotics for UTIs include TMP-SMX, trimethoprim, nitrofurantoin, fluoroquinolones, amoxicillin, co-amoxiclav and cephalosporins. Parenteral antibiotics are indicated for patients who are unable to tolerate oral therapy, have absorption problems or are infected with pathogens resistant to oral options. Aminoglycoside, with or without ampicillin, cephalosporins or fluoroquinolone, is recommended depending on bacteria susceptibility (Blair 2007). Appendix 1 lists examples of antibiotics suitable for use in elderly patients with UTIs with different routes of administration, doses and intervals.

### 1.5.8 AMR in UTIs

More resistant bacteria are often isolated in UTIs in elderly patients as a result of repeated exposure to antibiotics and urologic interventions (Nicolle 2009c). In the USA, a retrospective case series study of 435 UTI patients aged 16 or older was conducted to describe resistance patterns of infecting organisms and determine risk factors for multiple drug resistance. The multivariate analysis showed that all patients aged 65 or greater who used a urinary catheter and had recently used antibiotics had increased risk of infection with multiple drug-resistant bacteria (Wright *et al.* 2000).

Several studies have shown increased antibiotic resistance levels in community-acquired UTIs in general populations including the elderly (Barrett *et al.* 1999, Farrell *et al.* 2003, Bean *et al.* 2008, Jones *et al.* 2015). However, some researchers have suggested that these studies were subject to selection bias because the empirical UTI therapy started before the culture and sensitivity tests came back or because the decision to prescribe in some cases was based on MSU (Butler *et al.* 2006, Marques *et al.* 2012, Vellinga *et al.* 2012). In many countries, more than 20% of UTI causative bacteria are resistant to first-line UTI antibiotic therapy such as TMP-SMX, cephalosporins and even fluoroquinolones with resistance rates increased to 10% as reported in two surveys aimed at estimating the microbial susceptibility of uropathogens over years (De Backer *et al.* 2008, Schito *et al.* 2009). In the UK, there is a lack of nationally collated data on resistance levels in pathogens identified among urine specimens in primary care (Hayward *et al.* 2007). This is particularly concerning given the dramatic increase in cefotaxime and ceftazidime resistance in *E. coli* bacteraemia because of the emergence of extended spectrum beta-lactamase (ESBL) producing strains. Moreover, there has also been a marked increase in quinolone resistance in *E. coli* and other *Enterobacteriaceae* from bacteraemia (Hayward *et al.* 2007).

In 1997, a study to determine the sensitivities of urine isolates to eight commonly used antibiotics in general practice in 12 different laboratories in the UK examined 962 community acquired urinary bacterial isolates. The predominant isolated uropathogen was *E. coli* in 65.1% (N = 626) of the samples, followed by 23.4% (N = 225) *'coliforms'* other than *E. coli*, 4.6% (N = 44) *Proteus* and *Morganella* species, 2.4% (N = 23) *Enterococci*, 1.8% (N = 17) *Pseudomonas* species, 1.5% (N = 14) coagulase-negative *Staphylococci*, 0.7% (N = 7) group B *Streptococci* and 0.5% (N = 5) *Staphylococcus aureus*. As for sensitivity, 98.9% (N = 951) of all isolates were found to be sensitive to norfloxacin and to ciprofloxacin, 95.7% (N = 921) to co-amoxiclav, 86.8% (N = 835) to nitrofurantoin, 77.4% (N = 745) to cephalexin, 75.6% (N = 727) to trimethoprim, 75.0% (N = 722) to cephradine and 51.7% (N = 497) to amoxicillin. Furthermore, there was some variation in sensitivities among laboratories, mostly by overestimating nitrofurantoin and cephalosporins sensitivities and underestimating quinolones and co-amoxiclav sensitivities (Barrett *et al.* 1999).

Another UK multicentre study to determine the distribution of uropathogen resistance to antibiotics used to treat UTIs between 1999 and 2000 included 1,291 uropathogen isolates from eight centres in the UK. The isolates were cultured from four different groups: patients with community-acquired UTIs and younger than 65 (N = 397, 30.75%), patients with community-acquired UTIs and older than 65 (N = 392, 30.36%), patients with hospital-acquired UTIs other than those admitted with pyelonephritis (N = 394, 30.52%) and patients with hospital-acquired pyelonephritis (N = 108, 8.37%). The results showed that *E. coli* was the predominant uropathogen in all four groups; however, the percentage for each group varied. For example, it was 77.3% for patients younger than 65 with community-acquired UTIs versus 66.6% for patients older than 65 with community-acquired UTIs. Overall, amoxicillin's susceptibility against *E. coli* was 51.3%. It was greatly reduced because of beta-lactamase production and only partially restored by the addition of clavulanic acid with a susceptibility rate of 78.8%. Oral cefuroxime was active against *E. coli* by 68.6%; however, cefuroxime was inactive against both *Pseudomonas* and *Enterococcus* species. Nitrofurantoin was very active against *E. coli* isolates by 96.3% as well as *Enterococcus faecalis*, but not against *Klebsiella pneumoniae*, *Proteus mirabilis* or *Pseudomonas aeruginosa*. Overall, susceptibility to trimethoprim was 58.1%–84.5% for the most prevalent pathogens. Ciprofloxacin was highly active with susceptibilities of 88.6%–97.7% for the most prevalent pathogens including *E. coli* with a 97.7% susceptibility rate. It was the only oral agent tested against *Pseudomonas* species (Farrell *et al.* 2003).

Another study in East London sought to determine the level of bacterial resistance among all *E. coli* isolates collected from both the community and hospitals against eight commonly used antibiotics – ampicillin, co-amoxiclav, cefalexin, ciprofloxacin, gentamicin, nitrofurantoin, trimethoprim and cefpodoxime – over a 12-month period. Any samples collected from general practice, emergency or other primary care surgeries were considered representative of community isolates; whereas samples collected from patients hospitalised for 48 hours or more on general or specialised wards were considered hospital representative. The study successfully cultured 11,865 *E. coli* isolates over the study period, of which 88.7% (N = 10,521) were from the community. The results for *E. coli* resistance for the eight community antibiotics were: ampicillin 53.9%, co-amoxiclav

12%, cephalexin 8.3%, ciprofloxacin 9.3%, gentamicin 4.6%, nitrofurantoin 5.3%, trimethoprim 39.1% and cefpodoxime 5.7%. Multiple drug resistance was rare in the isolates; however, resistance to cefpodoxime indicated positive ESBL production in the community with higher extent in the hospital isolates. The study suggested that resistance to commonly used empirical oral antibiotics for UTI therapy was extremely high except for nitrofurantoin. Furthermore, the high level of *E. coli* resistance to ampicillin and trimethoprim has made them inappropriate oral antibiotics for empirical therapy (Bean *et al.* 2008).

In the UK, retrospective analysis of 70,313 uropathogen isolates took place across West London between April 2009 and March 2012 to recognise the susceptibility patterns in uropathogens against co-amoxiclav, gentamicin ,cephalexin, nitrofurantoin, ciprofloxacin and trimethoprim. The study collected isolates from more than 100 community practices (N = 38,768; 55.14%) and 1,600 beds from secondary care hospitals (N = 31,545, 44.86%). All collected isolates were requested based on clinical suspicion of UTI. The results showed that *E. coli* was the predominant uropathogen in 60.2% (N = 23,338) of the community isolates and 47.7% (N = 15,047) of the secondary care isolates. In respect of uropathogen susceptibility, the study detected a small fall in the antibiotics susceptibility rate from 2009–2010 to 2010–2011, followed by some recovery in 2011–2012 (primary care 94% in 2009–2010, 86% in 2010-2011 and 90% in 2011–2012; secondary care 91% in 2009–2010, 82% in 2010–2011 and 87% in 2011–2012). The reported susceptibilities for primary care were 75%–80% for co-amoxiclav, 86% for ciprofloxacin, 67% for trimethoprim, 88% for gentamicin and 94% for nitrofurantoin; whereas the susceptibilities for secondary care were 79% for ciprofloxacin, 60% for cefuroxime, 81% for cephalexin, 45%–60% for TMP-SMX, 82% for gentamicin and 92% for nitrofurantoin (Jones *et al.* 2015).

In Europe, a study of 908 *E. coli* urine cultures from Austria, Greece, Portugal, Sweden and the UK showed different rates of *E. coli* resistance for different antibiotics including trimethoprim, co-amoxiclav, TMP-SMX, nitrofurantoin and ciprofloxacin (Kahlmeter and Poulsen 2012). A 2014 WHO global surveillance report showed that five of the six WHO regions (Region of the Americas/Pan American Health Organization, Eastern Mediterranean Region, European Region, South-East Asia Region, and Western Pacific Region) reported more than 50% *E. coli* resistance to commonly used antibiotics, particularly fluoroquinolones and third-generation cephalosporins (Aarestrup *et al.* 2014).

Thus, the changing epidemiology and resistance patterns of UTI bacteria are making effective treatment of UTIs more difficult. The findings indicate that ciprofloxacin and co-amoxiclav remain reasonable options for UTI treatment in the UK. However, the rates of fluoroquinolone and co-amoxiclav resistance suggest that prudent use of these agents is necessary. *E. coli.* resistance to nitrofurantoin continues to be low compared with ciprofloxacin and co-amoxiclav. However, nitrofurantoin might not be a good choice for patients infected with *Enterobacteraciae* species, as these may have intrinsic resistance to it (Rowe and Juthani-Mehta 2013).

If an elderly patient with a UTI was thought to be infected with a resistant pathogen, it may be appropriate to use a combination of antibiotics from different classes (Chen *et al.* 2013). The rationale behind this approach is to increase the likelihood that the administered antibiotics are effective against the known or suspected pathogen. However, caution must be exercised regarding the possibility of increased toxicity, additional cost and further resistant in susceptible pathogen. In general, this approach may be appropriate for empirical antibiotic therapy when the elderly patient is severely infected, as the regimen can be narrowed to a single effective antibiotic once a pathogen is isolated, cultured, identified and susceptibility results are available (Bolon and Weber 2009).

### 1.5.9 Overview of UK Guidelines for UTI Treatment

Clinical practice guidelines (hereafter referred to as guidelines) have been developed to help HCPs make decisions about the care of their patients, evaluate and audit clinical practice, reduce inappropriate variations in clinical care, minimise harm and promote cost-effective practice (Watine *et al.* 2014).

In the UK, HCPs can access various guidelines either online or in hard copy. The British National Formulary (BNF) routinely encloses therapeutic guidelines from NICE, the Scottish Medicines Consortium (SMC) and SIGN. BNF recommendations are always checked against guidelines produced by expert organisations (Wright *et al.* 1999, Colodner *et al.* 2008). Access to infectious diseases-related recommendations, guidelines and reports can be retrieved from the PHE website. Other sources from which to retrieve guidelines include the NICE and SIGN websites. Additionally, each CCG publishes its own local prescribing policies, microbiology and antibiotics guidance as well as local prescribing formulary to assist and control GPs' prescribing decisions and cost (Knowles and Bliss 2014).

Worldwide, only eight guidelines for the treatment of UTIs in adults are written in English and listed by the Guidelines International Network (G-I-N), which includes 1,000 organisations from 48 countries (Henig *et al.* 2013, G-I-N 2015). Only one guideline represents the UK in this group: that published by SIGN in 2006 then updated in 2012 (SIGN 2012). It provides evidence-based recommendations for managing community-acquired UTIs in adults and includes adult females (including pregnant females) and males, patients with in-dwelling catheters and patients with co-morbidities such as DM. However, the guideline does not take into account prophylaxis to prevent UTIs after instrumentation or surgery, or treatment of recurrent UTIs (SIGN 2012). In 2015, PHE published a *'Management of Infection Guidance for Primary Care for Consultation and Local Adaptation'* that contained UTIs; however, it was only a summary of other national evidence-based recommendations from different organisations such as SIGN, NICE and NICE Clinical Knowledge Summaries (CKS). This guidance was first produced in 2000 and was updated regularly (McNulty 2015).

UK guidelines recommend first-line lower UTIs (LUTIs) therapy to be nitrofurantoin or trimethoprim for three days in females and seven days in males. Amoxicillin, ampicillin or cephalosporin may be used as second-line therapy. In the case of acute pyelonephritis, first-line therapy includes co-amoxiclav or broad-spectrum cephalosporin for 10 days for uncomplicated cases and 14 days for complicated ones. Alternatively, GPs might prescribe ciprofloxacin for seven days (JFC 2012, SIGN 2012, McNulty 2015). Table 12 summarises the treatment recommendations of different UK organisations and agencies for UTIs in adults.

Table 12: Summary of the different UK agencies' treatment guidelines for adults with UTIs

| | Treatment choices | |
|---|---|---|
| **Type of UTIs** | **First-line** | **Second-line** |
| **Uncomplicated UTI in males and (non-pregnant) females, no fever or flank pain** **(SIGN 2012, NICE 2014, McNulty 2015, NICE 2015b).** | **Nitrofurantoin:** 50-100mg every 6 hours orally **OR** 100mg Modified Release every 12 hours orally for 3 days in female and 7 days in male **OR** **Trimethoprim** 200mg every 12 hours orally for 3 days in female and 7 days in male | -Perform culture in all treatment failures. -Further treatment should be based on culture results. -If further empirical treatment is necessary consider nitrofurantoin (if failed on trimethoprim). -If failed on nitrofurantoin consider an oral first generation cephalosporin. |
| **UTI in pregnancy** **(SIGN 2012, McNulty 2015, NICE 2015b).** | **Nitrofurantoin:** 50mg every 6 hours orally **OR** 100mg Modified Release every 12 hours orally for 7 days. | **Cefalexin** 500mg every 12 hours orally OR 250mg every 6 hours orally for 7 days. If upper tract/systemic symptoms treat for 10-14 days. |
| **Acute Pyelonephritis** **(SIGN 2012, NICE 2013, McNulty 2015).** | **Co-amoxiclav** 625mg every 8 hours orally for 14 days. | **Ciprofloxacin** 500mg every 12 hours orally for 7 days. |
| **Catheter associated UTI*** **(SIGN 2012, McNulty 2015).** Symptomatic Patients Only* | **Presumed Upper Tract Infection or Presumed Bacteraemia:** **Co-amoxiclav** 625mg every 8 hours orally **OR** **Ciprofloxacin** 500mg every 12 hours orally **OR** – If sensitivity has been shown previously: **Trimethoprim** 200mg every 12 hours orally for 7-14 days. | **If known previous MRSA Bacteriuria:** **Trimethoprim** 200mg every 12 hours orally for 7 days. Do NOT use co-amoxiclav or quinolones owing to resistance. |
| **Proven Recurrent UTI in non-pregnant females ≥3/year** **(McNulty 2015, NICE 2015b)** | **Prophylactic for 6-month trial:** **Nitrofurantoin:** 50mg-100mg every night orally **OR** STAT post-coital dose to be taken within 2 hours of intercourse (off-label use) **OR** **Trimethoprim:** 100mg every night orally OR STAT post-coital dose to be taken within 2 hours of intercourse (off-label use) | |

The majority of practice guidelines do not adequately address elderly people in relation to use of different drugs, patient assessment or decision-making (Singh and Bajorek 2014). A recent UK Study evaluated 12 national guidelines and identified a potential for drug-disease and drug–drug interactions, especially in patients with co-morbidities, if the recommendations in these guidelines were adhered to (Dumbreck *et al.* 2015). Although this study included guidelines for chronic conditions, the authors highlighted on the importance of considering recommendations for drugs used for acute conditions like antibiotics. Unfortunately, none of the available guidelines for UTIs explore or address treatment options for elderly patients visiting GP surgeries appropriately as compared with other age groups (Beveridge *et al.* 2011, Cohen *et al.* 2011). Furthermore, all the recommendations for therapeutic regimens listed in the guidelines have been extrapolated from existing recommendations for adult populations and adult guidelines such as SIGN and IDSA/ESMID (Gupta *et al.* 2011) or cited as reference guidelines for elderly patients (Matthews and Lancaster 2011, Nicolle 2011, Rowe and Juthani-Mehta 2013).

In 2013, the Scottish Antimicrobial Prescribing Group (SAPG), an SMC group, published a decision-aid document for diagnosing and managing suspected UTIs in older people, containing summary lists adopted from PHE and SIGN recommendations for adults (SAPG 2013). It listed good practice points for obtaining urine culture, antibiotic therapy prescribing and managing prophylaxis in UTIs, all of which were particularly specific to older people at increased risk of developing ADRs. Further, the document emphasised the importance of avoiding broad-spectrum antibiotics such as ciprofloxacin, co-amoxiclav and cephalosporins since the elderly are more vulnerable to infection, particularly *Clostridium difficile* infection. It also discussed avoiding development of AMR; the benefits of using culture testing to guide appropriate prescribing; and using cranberry for prophylaxis rather than antibiotics for elderly patients (SAPG 2013). For the complete document see Appendix 2.

Despite the great efforts that have been invested into creating guidelines such as identifying evidence, assessing evidence quality and determining the strength of each statement (Wolf *et al.* 2011), they are often not followed by GPs (Cabana *et al.* 1999, Lugtenberg *et al.* 2009). In the UK, as in many other European and North American countries, GPs do not always adhere to antibiotic prescribing guidelines, which may result in negative consequences such as AMR and reduced health outcomes (Jelinski *et al.* 2005, Murphy *et al.* 2012). Several barriers and factors such as lack of familiarity, lack of awareness and lack of agreement have been found to hinder GPs' adherence to guidelines as reported by one systematic review and meta-synthesis aimed to explore GPs' attitudes to and experiences with regard to guidelines (Carlsen *et al.* 2007) and another systematic review aimed to identify barriers preventing GPs from adhering to guidelines (Cabana *et al.* 1999). The expanding body of research, workloads and time pressures made it difficult for GPs to be aware of and follow every applicable guideline (Cabana *et al.* 1999). Although there is wide awareness of many guidelines, a good number of GPs are unaware of their existence owing to factors such as volume of information, guideline accessibility and lack of time (Casey 2013). Moreover, awareness of guidelines does not guarantee familiarity with recommendations or ability to apply them correctly. GPs may not agree with a specific guideline or the concept of guidelines in general owing to applicability to patients, lack of confidence in guideline developers, their being '*too cookbook*' or too rigid to apply, biased synthesis and challenge to autonomy (Casey 2013). Several studies have explored how well GPs follow UTI guidelines for adults and the results confirm the general lack of adherence (Taur and Smith 2007, Lugtenberg *et al.* 2010, Llor *et al.* 2011). However, none of these studies have focused on GPs' adherence to guidelines in the case of elderly patients. Since evaluation of GPs' adherence to UTI treatment good practice points in the UK is one of this thesis' main objectives, relevant studies are discussed in more detail in Chapter Two.

### 1.6 Summary

This chapter has brought together a general overview of antibiotics prescribing in primary care, along with ageing and ageing-associated issues in respect of antibiotics and UTIs as some of the most common infections in this population worldwide. Considering that UTIs have gained their importance in elderly populations because of their high incidence and prevalence, it is no surprise that they are one of the most common reasons for GP surgery visits and antibiotics prescribing, with a high rate of recurrences and frequent administrations of antibiotics in the same person (Reeves 1994, Petersen and Hayward 2007a). Additionally, UTIs have been found to be over-diagnosed and over-treated in elderly populations in primary care settings on the basis of atypical patient presentation (Beveridge *et al.* 2011). Moreover, there is growing global concern about LUTIs that responded readily to oral antibiotics in the past, but that now may need to be treated with injected antibiotics – imposing additional costs on patients and healthcare systems – or become untreatable (Aarestrup *et al.* 2014). Since elderly people have several issues such as ageing-associated physiological changes, atypical UTI presentations, infections with more resistant pathogens, multi-morbidities or co-morbidities and polypharmacy, UTIs are unique in this population. Therefore, it is important for GPs to understand more about their current antibiotic prescribing practices in such a vulnerable age group to avoid inappropriate, perhaps wasteful and risky management that might squander resources, create iatrogenic problems, increase AMR and lead to negative clinical outcomes. The next chapter provides an in-depth and extensive literature review to inform this research and identify the limitations and gaps of the previously published research.

# Chapter 2 Literature Review

## 2.1 Introduction

The main aim of this chapter was to provide an extensive structured theoretical review of previously published studies and ongoing research that is closely linked and relevant to this thesis. The review was achieved through identifying, exploring and discussing the available information while highlighting the significance of relevant research and identifying gaps in the current knowledge (Cronin *et al.* 2008).

The chapter begins with a definition of a literature review and its objectives followed by details of the literature search strategy, inclusion and exclusion criteria and literature review process. Studies relevant to prevalence, antibiotic prescribing, adherence to guidelines and antibiotics prescribing behaviour and practice are all discussed from GPs' perspective in relation to elderly patients with UTIs. The limitations of these studies were also discussed to highlight further research opportunities. Finally, the thesis aims and questions are presented to target this research towards closing those identified gaps that are impairing the body of knowledge about GPs' antibiotics prescribing for elderly patients with UTIs.

## 2.2 Definition and Uses

A literature review can be described as a comprehensive study and interpretation of literature that relates to a particular topic (Aveyard 2014, p. 1). It may be used to influence different stages of the research process in both qualitative and quantitative research. In qualitative research, the literature review can be used to place the findings of the research within the context of what is already known, that is, it is not used to confirm or argue existing findings but instead to enlighten readers about how the research findings fit into the existing knowledge about the phenomenon under investigation (Speziale and Carpenter 2010). On the other hand, a quantitative research literature review may be used for different purposes such as (Aveyard 2014):

- suggesting a conceptual or theoretical framework;
- stating the research purpose;
- verifying the significance of the research problem;

- assisting in research design selection;
- clarifying the research topic or problem;
- describing relevant studies;
- summarising and evaluating current knowledge;
- guiding data collection and analysis;
- pinpointing assumptions and limitations; and
- assisting in interpreting findings.

In order to set up the research background context for this thesis, an extensive in-depth review of literature that described GPs' antibiotics prescribing for elderly patients with UTIs was undertaken.

## 2.3 Search Strategy

A computerised literature search was performed, which was driven by the thesis aims and research questions and focused on all relevant published works including peer-reviewed journals, books, websites, guidelines and professional-body publications. Additional searches were carried out to identify any *'grey'* literature sources, that is:

> *'Literature which is produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers'* (Farace and Frantzen 1998, p. iii).

Searched grey literature included theses, conferences, white papers and proceedings. Another search strategy was performed through the use of a snowball technique, where the references lists from relevant journals were searched to identify additional relevant literature. Literature searches were performed and updated constantly at different stages of the research to update the literature (Aveyard 2014).

Seven medical databases were searched for relevant literature. These databases were recommended by King's College London (KCL) library services and Aveyard for students and researchers undertaking research related to health and medicine (Aveyard 2014, KCL Library Services 2014). The searched databases included:

- National Library of Medicine (MEDLINE) including In-Process & Other Non-Indexed Citations;
- BioSciences Information Service (BIOSIS);

- Excerpta Medica Database (EMBASE);
- Cumulative Index of Nursing and Allied Health Literature (CINAHL);
- NICE Evidence Search;
- International Pharmaceutical Abstracts (IPA); and
- Cochrane Library Database of Systematic Reviews.

These electronic medical databases were used because of their relevance to the healthcare field. However, they cited only published literature. In order to avoid publication bias from impacting the research literature review, a search of grey literature databases was also performed using additional sources such as:

- Health Management Information Consortium (HMIC) database, which consists of two health management databases: Department of Health's DH-Data and King's Fund database;
- Online Computer Library Center (OCLC) WorldCat Dissertations and Theses database;
- Google Scholar;
- Web of Science; and
- OpenGrey (the system for information on grey literature in Europe).

All were searched for any publication or grey literature. The searched medical databases and additional sources were available from the KCL library's online portal. Potentially relevant literature was retrieved either manually or electronically or requested from the library interloan system and downloaded into Endnote®, publishing and managing bibliographies, *citations* and references software, version 7, Thomson Reuters Corporation, Philadelphia, USA.

## 2.4 Searched Terms

Five searches were performed to cover the four aspects of the research questions. The five searches focused on: 1) epidemiology of UTIs in elderly; 2) GPs' antibiotics prescribing for elderly patients with UTIs; 3) GPs' adherence to UTI recommendations for elderly patients; 4) GPs' views and perceptions of antibiotics prescribing for UTIs in elderly patients; and 5) factors influencing GPs' antibiotics prescribing for UTIs in adults and the elderly.

All searched keywords and search strategies were verified and confirmed by Medical Information Specialists from KCL library. For full search keywords used and search strategy, see Appendix 3. To ensure that all potentially relevant literature was identified, various search strategy enhancing techniques were used, including:

- searching for a combination of relevant keywords and their synonymous using free-text and *'medical subject heading'* (MeSH) terms with and without truncation ('$' or '*') to facilitate the inclusion of stem words;
- searching for phrases in quotation marks; and
- using the Boolean operators (AND, OR, NOT) to combine keywords.

## 2.5 Inclusion and Exclusion Criteria

Literature was considered relevant only if it met a list of inclusion criteria. Any literature failing to meet this list was excluded. Moreover, any study that failed to distinguish between the age of the studied population or between symptomatic UTIs and asymptomatic bacteriuria (ASB) was considered irrelevant as ASB does not require antibiotic therapy. The search inclusion and exclusion criteria that were used in this thesis can be found in Table 13. These criteria were used to serve this thesis' research questions and to narrow the search findings.

Table 13: Search inclusion and exclusion criteria for research approaches

| | **Quantitative research** | | **Qualitative research** | |
|---|---|---|---|---|
| | **Epidemiology** | **Drug utilisation** | **Variations in views and perceptions** | **Factors influencing prescribing** |
| **Inclusion** | English | English | English | English |
| | Quantitative | Quantitative | Qualitative | Qualitative |
| | Any country | Any country | Any country | Any country |
| | Between 2000-2015 | Between 2000-2015 | Between 2000-2015 | Between 2000-2015 |
| | Elderly | Elderly | Elderly | Elderly |
| | Primary care/GPs | Primary care/GPs | Primary care/GPs | Primary care/GPs |
| | UTIs | UTIs | UTIs | UTIs |
| | With abstract or full text | With abstract or full text | With abstract or full text | With abstract or full text |
| **Exclusion** | None English | None English | None English | None English |
| | Qualitative | Qualitative | Quantitative | Quantitative |
| | Before 2000 | Before 2000 | Before 2000 | Before 2000 |
| | None elderly | None elderly | None elderly | None elderly |
| | ASB, catheterised | ASB, catheterised | ASB, catheterised | ASB, catheterised |
| | Hospital<br>LTCF<br>Nursing home<br>Institutionalized<br>ED<br>Surgical units<br>HCAI | Hospital<br>LTCF<br>Nursing home<br>Institutionalized<br>ED<br>Surgical units<br>HCAI | Hospital<br>LTCF<br>Nursing home<br>Institutionalized<br>ED<br>Surgical units<br>HCAI | Hospital<br>LTCF<br>Nursing home<br>Institutionalized<br>ED<br>Surgical units<br>HCAI |

ASB: Asymptomatic bacteriuria; LTCF: Long term care facilities; ED: Emergency departments; HCAI: Healthcare-associated infection

## 2.6 Literature Review Process

All retrieved literature abstracts and full texts were screened to identify any duplication and determine the relevance to the research inclusion criteria. This was achieved through screening literature titles, abstracts and content using a pragmatic process. This process was ongoing and continuous during the literature search and update process. Studies were considered for inclusion in the review if they:

- provided an abstract or full text (the decision was made based on the literature content);
- abstract or full text contained these keywords *'GPs'*, *'antibiotic'* and *'urinary tract infection'* or their synonyms; and
- abstract or full text contained substantial detail about the method used, that is, *'qualitative'*, *'interview'*, *'drug utilisation'*, *'observational'*, *'cross-sectional'* and *'epidemiological'*.

All literature deemed to be directly relevant to the research was explored and critically appraised later in this chapter (Coughlan *et al.* 2007, Ryan *et al.* 2007, Aveyard 2014). Searches were repeated at least once every four months, with regular checks for newer literature that might have been published or cited after the initial or previously updated search. The final literature update was done on 1 February 2016, identifying one article.

All relevant literature was critically appraised using the Critical Appraisal Skills Programme (CASP) check list recommended by KCL and available at: (www.casp-uk.net/#!casp-tools-checklists/c18f8). This tool was developed by the Public Health team and the programme of the North Thames Research Appraisal Group (NTRAG) in Oxford in 1993. CASP is for new researchers and those who require quick, simple and easy-to-understand tools for appraising different types of literature such as qualitative research and cohorts (Taylor *et al.* 2004, Singh 2013).

## 2.7 Literature Review Results and Discussion

The search identified a few similar research though not with identical inclusion and exclusion criteria. The lack of identical research especially in the UK was also confirmed by KCL Medical Information Specialists after an independent literature search. The search was thus expanded to include any published research since 1995 with mixed study settings or mixed patient ages as long as results relating to elderly people were distinguished from other age groups. If this was not possible, published research on the general population in primary care was included to inform the research about the current situation. Figure 12 illustrates the expanded approach used in this thesis. This section summarises the identified literature followed by discussion and rationale for research.

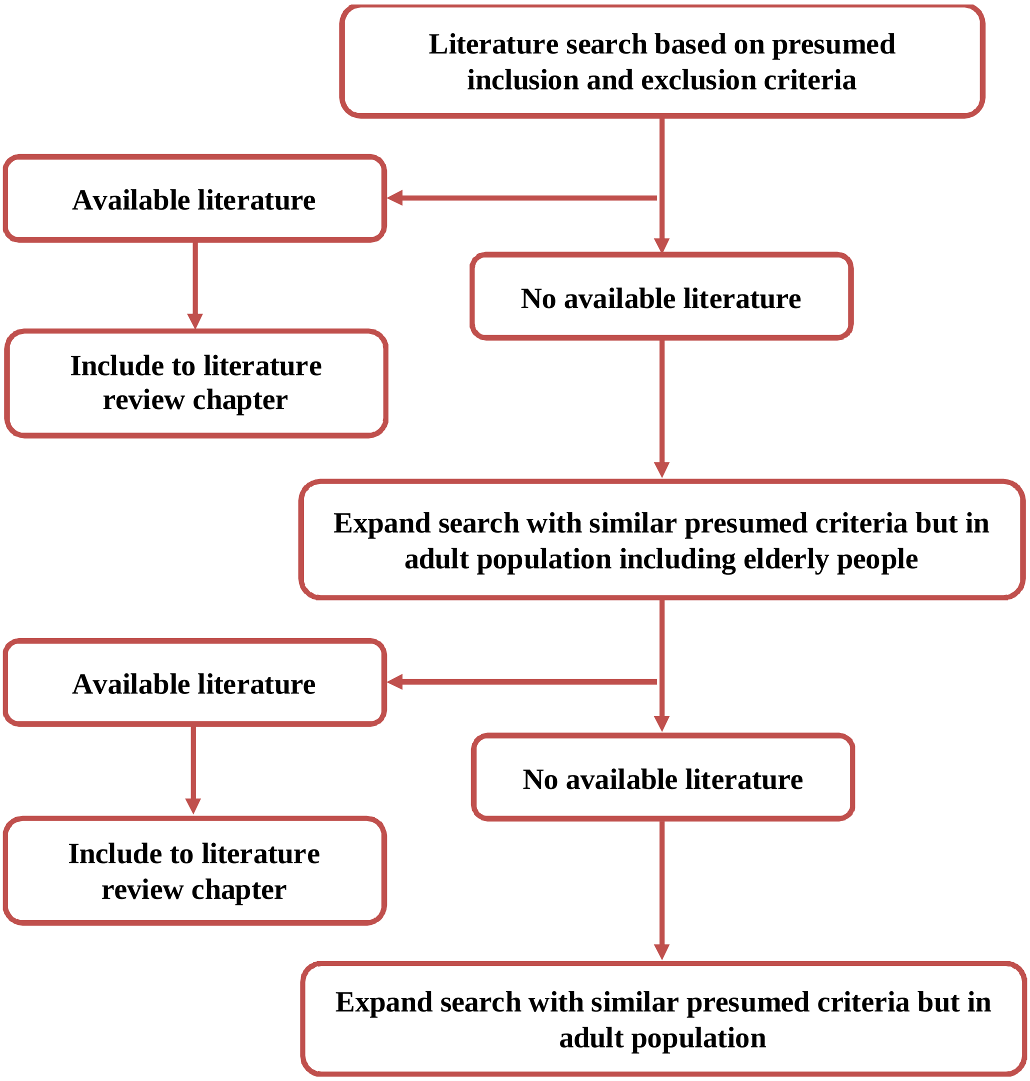



Figure 12: Expanded approach for literature inclusion

### 2.7.1 Literature Review Results

### 2.7.1 The Epidemiology of UTIs in Elderly Patients

The epidemiology of UTIs in the elderly can be challenging (Stamm and Norrby 2001) for many reasons: the atypical UTI presentations of elderly people compared with other age groups; the difficulty of differentiating between symptomatic UTIs and ASB, which can lead to disease misclassification; and the lack of a universally accepted definition and diagnostic criteria for UTIs in the elderly. Although there was a considerable amount of literature on the epidemiology of UTIs, the diagnostic criteria adopted across these studies varied significantly, which might result in either under- or overestimation of the epidemiology of UTIs (Rowe and Juthani-Mehta 2013, Rowe and Juthani-Mehta 2014, Detweiler *et al.* 2015).

As at younger ages, it has been found among elderly people that UTI incidence was higher in the female gender with the female-to-male ratio ranging between 2:1 (Wilson and Markland 2014) and 3:1 (Nicholl and Wilson 2012). This is explained by females having a shorter urethra compared with males. In addition, males can have antibiotic substances in their prostatic fluid that act as a natural defence mechanism against infection (Foxman 2010). Although the prevalence of UTIs increases substantially with advancing age for both males and females (Nicolle 1994), the female:male infection ratio falls with advancing age from 30:1 cases in younger adults to 2:1 cases in those aged over 65 (Schaeffer 1991). The literature review identified 12 studies on the epidemiology of UTIs in elderly patients that were reviewed and critiqued in the next paragraphs and summarised in Table 14.

In the USA, a prospective, observational epidemiological study aimed at estimating the incidence and possible risk factors of infections in non-institutionalised, urban elderly people aged 65 and over between July 1986 and June 1988 recruited 417 elderly people from two local healthcare centres. Of the participants, 33% (N = 138) were male and 67% (N = 279) were female, with the majority younger than 74 (N = 254, 61%). Over the 24-month period, all recruited elderly people were asked to complete a form listing 26 symptoms every time they visited or phoned a clinic or hospital for an infection. The study recorded 494 infections and UTIs were the second most common type of infection after colds with a total of 93 (18.83%) representing an overall incidence of 13 per 100 persons per year. Female incidence was higher compared with male with rates of 14 per 100 persons per year and 10.9 per 100 persons per year, respectively, with no statistical significance. From an age perspective, UTIs were higher in elderly people younger than 74 with an incidence of 15.1 per 100 persons per year compared with 11.6 per 100 persons per year for those aged 74 and older. This study was the first to explore the incidence of infectious diseases in elderly people aged 65 and older and not in nursing homes. Also, it successfully demonstrated that infectious diseases are common and vary a lot among the elderly. However, it did have significant limitations related to infection symptoms in this population, in particular for UTIs, where symptoms and presentations can be atypical and distinguishing between UTIs and ASB is difficult. In addition, screening for infection in this study was based on symptoms reporting rather than on clinical examinations or laboratory tests, which might have resulted in incidence bias for some conditions. Moreover, some infections might have been incompletely captured owing to their nature or to certain elderly co-morbidities or diseases potentially associated with clinical presentations that could be similar to the clinical presentations of infections, leading to wrong diagnosis (Ruben *et al.* 1995).

A cohort study using a postal questionnaire was undertaken in Sweden to estimate the prevalence of urinary incontinence and other urogenital symptoms including UTIs in a random sample of 10,458 male patients aged 45 and older, 74% (N = 7,763) of whom completed the questionnaire successfully. Results revealed that UTI prevalence within the previous 24 months among the responded sample for ages 65, 70, 75, 80, 85–89 and 90 years and older was 6.4% (N = 500), 4.5% (N = 349), 8% (N = 621), 10.7% (N = 831), 13.9% (N = 1,079) and 16.5% (N = 1,281), respectively. Additionally, the prevalence of UTIs was found to increase significantly with advancing age ($p < 0.001$) with the highest prevalence identified among elderly people aged 90 and above. Although the study successfully linked ageing with high prevalence of UTIs in males, this prevalence may have been under- or overestimated because the study included patients from mixed care settings. Furthermore, the prevalence calculation was based on a self-reported questionnaire with no diagnostic or microbiological investigations to confirm the diagnosis of UTIs or to distinguish UTIs from ASB, which was treated by antibiotics at that time (Malmsten *et al.* 1997).

Another Swedish longitudinal cohort study sought to estimate the prevalence of UTIs, urinary incontinence, oestrogen use and overall mortality in female patients aged 66 to

86 who received antibiotic treatment for UTIs in the period between 1985 and 1986 with a follow-up re-estimation of UTI prevalence for the same studied group in 1995. In 1986, 6,000 female participants were invited to complete a questionnaire about urogenital complaints. Only 70% (N = 4,206) completed the questionnaire successfully and, of those, only 16.36% (N = 688) reported receiving antibiotic treatment for UTI between 1985 and 1986. Ten years later, 63% (N = 434/688) of the females were still alive and were invited to participate in a second questionnaire about urogenital complaints. This time 83% (N = 361) completed the questionnaire successfully, of whom 61% (N = 219) reported receiving antibiotic treatment for at least one UTI within the last nine years. The number of reported UTI episodes varied: 35% (N = 77) had one to two, 28% (N = 61) had three to four, 27% (N = 59) had five to 10 and 10% (N = 22) had more than 10. Although the study positively linked high UTI occurrence in elderly females having had previous episodes, it could not establish an association between UTIs and increased mortality in the elderly. In terms of weaknesses and limitations, first, the study did not identify the care settings of patients from which the 1986 questionnaire responses were received as UTI prevalence can differ dramatically from one setting to another. Second, it included responses from mixed care settings in 1995 and analysed them collectively, which may have led to bias in prevalence estimation. Third, the study did not compare the findings about UTI prevalence with any previously published work. Fourth, it was based totally on questionnaires, which might make respondents subject to bias. Finally, UTI prevalence in this study may have been under- or overestimated because there were no diagnostic or microbiological results to confirm the diagnosis of UTIs or to distinguish UTIs from ASB, which was treated by antibiotics at that time (Molander *et al.* 2000).

In the USA, survey analysis covering March 1995 through February 1996 aimed at estimating the annual incidence, age cumulative probability and direct medical and non-medical associated social costs for over age 18 female participants with UTIs using random phone number dialling for data collection. Estimated results showed that 180 females aged 65 and older (9%) reported a single UTI during the last 12 months, of whom 20 (1%) reported a first lifetime UTI during those 12 months. What is more, UTI incidence was not found to increase with age among elderly females. Although this investigation was one of the first to determine the incidence and associated social costs of UTIs, it had limitations, a major one of which was recall bias for either the diagnosis or the timing of the diagnosis or both. Another was the failure to compare the findings regarding prevalence with previous literature and a third was not considering co-morbidities and risk factors, since the presence of these can either over- or underestimate the incidence, making the results subject to bias (Foxman *et al.* 2000).

In South Korea, a 2004 retrospective study sought to determine the incidence, recurrence, seasonality, mortality and medical costs associated with acute pyelonephritis in outpatient and inpatient settings between 1 January 1997 and 30 September 1999 using their nationwide health insurance claims database. The database recorded 496,289 claims for acute pyelonephritis diagnosis: 164,661 claims in 1997, 166,436 claims in 1998 and 165,192 claims in 1999. Female patients had higher overall outpatient incidence with 49.1 per 10,000 populations compared with 11.4 per 10,000 populations for male patients. The average annual outpatient incidence for females was 57.15 per 10,000 populations for the 60–79 age group and 28.07 per 10,000 populations for the 80 and over age group; while for outpatient males the average incidence was 20.51 per 10,000 populations for the 60–79 age group and 25.10 per 10,000 populations for the 80 and over age group. Acute pyelonephritis incidence among male outpatients was found to increase gradually with advancing age, reaching its peak at the age of 80 and over. The incidence among female outpatients was found to decrease sharply from the age of 80. The ratio of outpatients to inpatients was higher for males than for females but decreased with age for both genders. The study proved that acute pyelonephritis occurs more frequently in elderly patients aged 60 years or older compared with other age groups; female outpatient acute pyelonephritis incidence was five times higher than for inpatient treated females and 10 times higher than for males. The study showed some limitations related to the validity of the insurance database, which was not established, in addition to diagnosis reliability for retrieved cases. It was also subject to bias in estimating UTI incidence for several reasons such as the lack of clinical data and laboratory tests from the insurance database, disease misclassification and imprecise use of the disease classification system resulting in incomplete capture of all cases and the antibiotics purchasing policy in South Korea, which until 2000 allowed individuals to purchase antibiotics without a prescription (Ki *et al.* 2004).

Galatti *et al.* (2006) conducted a retrospective analysis to identify Italian GPs' antibiotics prescribing patterns as well as patient-related variables associated with prescriptions for acute and recurrent cystitis in the general population using the Health Search Database (HSD), an Italian GP research database, between 1999 and 2002. The study included 35,129 cases, of which 31.35% (N = 11,013) were elderly patients aged over 65. The prevalence of acute complicated cystitis in elderly patients was 50.1% (N = 10,266) of the total number of acute complicated cystitis cases in the general population, whereas the prevalence of recurrent cystitis was 53.2% (N = 747) of the total number of current cystitis cases. Elderly patients were more likely to receive antibiotic treatment for both conditions with 81.0% (N = 8,313) for acute complicated cystitis (OR[16]: 1.63; 95% CI 1.43–1.86) and 85.5% (N = 6,39) for recurrent cystitis (OR: 1.96; 95% CI 1.39–2.76). Although Galatti *et al.*'s (2006) study confirmed the high prevalence of both acute complicated and recurrent cystitis in elderly patients compared with other age groups, it had significant limitations related to imprecise use of the disease classification system, disease misclassification, incomplete capture of all cases and missing laboratory data for some patients (Galatti *et al.* 2006).

Czaja *et al.* (2007) carried out a population-based analysis in the USA from January 1997 to December 2001 intended to estimate acute pyelonephritis incidence, microbial aetiology, AMR and antibiotic therapy use for outpatient and inpatient settings using a computerised database from a health maintenance organisation. The data identified 4,887 individuals with 10,330 acute pyelonephritis diagnoses over the five-year study period. Elderly outpatient findings revealed that females had higher UTI incidence compared with males across all elderly age groups. Female outpatient incidence was estimated to be nine (expressed in 10,000 person-years) for the 65–69 age group, 11 for the 70–74 age group, 12 for the 75–79 age group, 13 for the 80–84 age group and 12 for the 85 and over age group. For male outpatients, the estimated incidence was five for the 65–69 age group, six for the 70–74 age group, seven for the 75–79 age group, five for the 80–84 age group and six for the 85 and over age group, all expressed in 10,000 person-years. Additionally, the outpatient UTI incidence rates for elderly patients were higher compared with the inpatient rates for both genders. Peak incidence was seen in outpatients aged 82 for females and 88 for males. Although this study demonstrated the relationship between pyelonephritis and ageing, it had significant limitations, including imprecise use of the disease classification system, disease misclassification, incomplete capture of all cases and missing laboratory data for some patients. Furthermore, the study mentioned that UTI incidence can vary substantially according to sex and age; however, no age–sex adjustment was performed for rates to eliminate their influence on incidence (Czaja *et al.* 2007).

[16] Odds ratio.

Laupland *et al.* (2007) performed a Canadian population-based, laboratory surveillance study to estimate community onset UTI incidence, demographic risk factors, AMR and aetiological pathogens among a non-selected large population using microbiology results from one laboratory between 2004 and 2005. Results revealed that elderly females had higher UTI incidence compared with males. The estimated incidence for females was 40 for those aged 60–69, 46 for those aged 70–79 and 110 for those aged 80–89, all expressed in 1,000 per year; whereas the estimated male incidence was 10 for those aged 60–69, 15 for those aged 70–79 and 60 for those aged 80–89, all expressed in 1,000 per year. The overall incidence in elderly people with UTIs was found to increase substantially with advancing age in both genders. The overall incidence per age group was 25 for those aged 60–69, 33 for those aged 70–79 and 100 for those aged 80–89, all expressed in 1,000 per year. Interestingly, elderly people who were 90 or older had the highest UTI incidence among all age groups with 925.7 for females, 637.8 for males and 850.6 overall per 1,000 per year. Although Laupland *et al.* (2007) had several interesting findings related to the increase in UTI incidence with advancing age, their study was limited by the lack of patients' clinical presentations to distinguish between different subclasses of UTI. Moreover, the study included microbiological cultures from community clinics, nursing homes and emergency departments in addition to samples from acute care hospitals for inpatients within their first two days of admission. Therefore, the incidence may have been biased since some of these settings are associated with high UTI incidence, not to mention the nature of patients who visit some of these settings as well as the severity of their conditions.

Eriksson *et al.* (2010) conducted a cross-sectional, population-based study in Sweden and Finland from 2005 to 2006 aimed at describing the prevalence of UTIs as well as the factors associated with them in a sample of 395 female patients aged 85 and older. Data were collected by nurses, physicians, medical students and physiotherapists through home visits and medical records review. Results showed that 29.6% (N = 117) of the participants were diagnosed to have had at least one UTI episode during the last 12 months. Estimated UTI prevalence per age was 25% (N = 33) of 85-year-olds, 29.6% (N = 35) of 90-year-olds and 34.4% (N = 40) of those aged 95 and over. Results for prevalence estimation were not shown to be statistically significant. Furthermore, 60% (N = 233) had at least one UTI diagnosis during the previous 60 months. Although the study identified UTI prevalence and associated risk factors, the prevalence might be overestimated as a result of including patients from different settings such as community clinics, nursing homes and hospitals. Another key fact was that patients from hospital setting tend to have more UTIs than community patients, especially if they are catheterised. Furthermore, the researchers did not consider collection of urine samples and microbial cultures during home visits to confirm UTI diagnoses.

Omoregie *et al.* (2010) carried out a study in Nigeria to determine the prevalence of UTIs among elderly patients aged 60 and older and visited different outpatient clinics in teaching hospitals from 1 September 2009 to 31 May 2010. Researchers collected clean-catch MSU from 943 patients with UTI signs and symptoms, of whom 61.62% (N = 581) were female and 38.38% (N = 362) were male. Results showed the overall estimated UTI prevalence to be 11.03%. Moreover, being of the male gender was found to be a significant risk factor for UTIs: 23.1% (N = 80) (OR: 6.584; 95 CI 4.081−10.62) versus 4.13% (N = 24) (OR: 0.152; 95% CI 0.094−0.245) in female elderly patients ($p < 0.0001$). Additionally, the study found that the prevalence of UTIs significantly decreased with advancing age from 14.46% for those aged 60−69, 10.94% for those aged 70−79, 8.26% for those aged 80−89 and 3.2% for those aged 90−99 ($p = 0.023$). Furthermore, the prevalence in this study might be biased as a result of the nature of patients who tend to visit hospital outpatient clinics who could have multiple co-morbidities, disabilities and severe illnesses as well as risk factors for developing UTIs. Moreover, the findings showed results that were inconsistent with previously published studies regarding gender and age without reasonable explanations. That said, some postulated justification might be the life expectancy of the Nigerian population, which is between 54 and 55 years according to WHO.

In the Netherlands, Caljouw *et al.* (2011) performed a population-based, prospective follow-up study of UTI incidence and predictive factors in elderly patients aged 85 between September 1997 and September 1999. The study included 479 patients, of whom 67.2% (N = 322) were female and 32.8% (N = 157) were male. Data were collected during researchers' visits to participants' places of residence. Results revealed that 15% (N = 72) of the participants had a history of at least one UTI episode between the ages of 85 and 86. Further analysis showed that 18.3% (N = 59) of female and 8.3% (N = 13) of male patients had a history of at least one UTI episode between the ages of 85 and 86 ($p = 0.004$). The overall reported incidence of UTIs was found to be 11.2 (95% CI 9.4−13.1) per 100 person-year at risk. The incidence of UTIs was greater in females with 12.8 (95% CI 10.4−15.2) per 100 person-year at risk than males with 7.8 (95% CI 5.1−10.6) per 100 person-year at risk. This significant result means that females had a 1.7-fold increased risk of developing UTIs compared with males (HR[17]: 1.7; 95% CI 1.1−2.5) ($p = 0.012$). Although this study successfully described the incidence and predictive risk factors, it had certain limitations. The old data used to estimate the incidence of UTIs did not represent the real incidence at the time of the study. Another key fact is that advancing age is often associated with changes in the immune system and urinary tract, which could explain the high incidence of UTIs in the elderly; therefore, more reflective estimates would have been provided by estimating the annual incidence of UTIs rather than one-point incidences. Another limitation related to UTI diagnosis, which was not performed in accordance with the standardised diagnostic procedures. Furthermore, the incidence in this study might be biased owing to overlapping between UTIs and ASB in addition to including institutionalised patients from long-term care facilities who are usually catheterised, which can increase the risk of developing UTIs and ASB and therefore overestimate the incidence of UTIs.

Marques *et al.* (2012) carried out a prospective, population-based study in Brazil to estimate the epidemiology and clinical characteristics of UTIs for community-dwelling females over the age of 65 from January to June 2010. This study included 598 female patients who were recruited during their first visit to a GP or nephrologist clinic at a university hospital. Results showed high prevalence of UTIs in the studied sample (N = 99; 16.55%) with significantly higher prevalence in older women ($p < 0.001$). Among the UTI cases, 97.98% (N = 97) presented with cystitis and 2.02% (N = 2) presented with pyelonephritis. Moreover, 28.28% (N = 28) had recurrent UTIs. From a therapeutic standpoint, nitrofurantoin was used as an oral therapy for seven days for all cystitis patients; while pyelonephritis patients were treated with intravenous co-amoxiclav followed by oral therapy for 14 days. This study successfully linked the prevalence of UTIs with ageing and previous UTI history. However, it had limitations. First, the sample size was small for a population-based study in addition to there being only a short period of follow-up. Second, the study recruited patients from a tertiary care hospital who tend to have multiple co-morbidities, risk factors, disabilities and severe conditions that might predispose these patients to UTIs more frequently and result in prevalence bias. Having said that, another potential source for prevalence bias was the exclusion of severely disabled patients' laboratory investigations.

[17] Hazzard ratio.

In conclusion, twelve studies were identified to estimate UTI epidemiology in elderly people, of which only nine described UTI epidemiology in general (Ruben *et al.* 1995, Malmsten *et al.* 1997, Molander *et al.* 2000, Galatti *et al.* 2006, Laupland *et al.* 2007, Eriksson *et al.* 2010, Omoregie *et al.* 2010, Caljouw *et al.* 2011, Marques *et al.* 2012), one studied cystitis (Ki *et al.* 2004) and two studied pyelonephritis (Foxman *et al.* 2000, Czaja *et al.* 2007). Six studies were designed specifically for the elderly population (Ruben *et al.* 1995, Molander *et al.* 2000, Eriksson *et al.* 2010, Omoregie *et al.* 2010, Caljouw *et al.* 2011, Marques *et al.* 2012) and the rest included elderly people as part of the studied population with three studies lacking a specified number of elderly people (Ki *et al.* 2004, Czaja *et al.* 2007, Laupland *et al.* 2007). Only four studies included female patients (Foxman *et al.* 2000, Molander *et al.* 2000, Eriksson *et al.* 2010, Marques *et al.* 2012), one included male patients (Malmsten *et al.* 1997) and seven included both genders. There were five studies from four European countries, namely, Sweden, Italy, Finland and the Netherlands (Malmsten *et al.* 1997, Molander *et al.* 2000, Galatti *et al.* 2006, Eriksson *et al.* 2010, Caljouw *et al.* 2011), three from the USA (Ruben *et al.* 1995, Foxman *et al.* 2000, Czaja *et al.* 2007), one from South Korea (Ki *et al.* 2004), one from Canada (Laupland *et al.* 2007), one from Nigeria (Omoregie *et al.* 2010), one from Brazil (Marques *et al.* 2012) and none from the UK. Six studies estimated UTI prevalence as a percentage (Malmsten *et al.* 1997, Molander *et al.* 2000, Galatti *et al.* 2006, Eriksson *et al.* 2010, Omoregie *et al.* 2010, Marques *et al.* 2012) whereas the other six studies expressed UTI incidence in different units. The studies varied in research design and data sources, ranging from questionnaires and surveys in four studies (Ruben *et al.* 1995, Malmsten *et al.* 1997, Foxman *et al.* 2000, Molander *et al.* 2000), databases in four studies (Ki *et al.* 2004, Galatti *et al.* 2006, Czaja *et al.* 2007, Laupland *et al.* 2007) and medical records in three studies (Eriksson *et al.* 2010, Caljouw *et al.* 2011, Marques *et al.* 2012) and one based on results from urine analysis alone (Omoregie *et al.* 2010). Only three studies considered laboratory results while taking into account culture and MSU analysis to confirm UTIs (Laupland *et al.* 2007, Caljouw *et al.* 2011, Marques *et al.* 2012).

Epidemiological studies might be subject to varied bias conceptualised through a lack of internal validity or incorrect assessment of the association between an exposure and an effect in the target population (Delgado-Rodriguez and Llorca 2004). Selection bias was a problem in some studies. The studies describing UTI incidence or prevalence based on urine sample detected UTIs in samples requested by the GP because they already suspected UTI (Laupland *et al.* 2007, Caljouw *et al.* 2011, Marques *et al.* 2012). This means that erroneous overestimation of the incidence or prevalence is possible because only those with a high likelihood of UTI were selected to form the population in the calculated UTI rate. Or the rate could be erroneously underestimated if clinical suspicion is a poor indicator of UTIs and many patients with UTIs were unselected, hence their UTIs went undetected. A number of studies failed to include a representative sample of elderly population from the community setting by including patients from other settings together with different age ranges, which complicates the interpretation and comparison of these rates (Malmsten *et al.* 1997, Molander *et al.* 2000, Laupland *et al.* 2007, Eriksson *et al.* 2010, Omoregie *et al.* 2010, Marques *et al.* 2012). Additionally, some studies did not report or consider patients with co-morbidities when they recruited them, as UTIs increase with the presence of certain co-morbidities such as DM (Ruben *et al.* 1995, Foxman *et al.* 2000). Self-reporting studies were subject to recall bias, especially in the elderly as this population group might have issues with memories and remembering events (Ruben *et al.* 1995, Foxman *et al.* 2000). Also, systematic differences in the recording or interpretation of data could cause interview bias (Eriksson *et al.* 2010, Caljouw *et al.* 2011). Another important consideration is UTI code misclassification bias. In the case of elderly people, given the problems with diagnosis, contamination, mixed cultures and ASB, a UTI could easily be misclassified as a non-UTI or vice versa (Laupland *et al.* 2007, Caljouw *et al.* 2011, Marques *et al.* 2012). Variations in defining UTIs over time as well as across guidelines and laboratories might result in rates being either over- or underestimated. In database studies, variations in coding, disease coding misclassification and incomplete capture of all UTI cases might influence the rate estimation (Ki *et al.* 2004, Galatti *et al.* 2006, Czaja *et al.* 2007, Laupland *et al.* 2007). Furthermore, a number of studies were limited by small sample size and therefore could not estimate prevalence or incidence rates precisely (Ruben *et al.* 1995, Eriksson *et al.* 2010, Caljouw *et al.* 2011). A criticism of studies that estimate epidemiology based on urine samples is that samples sent for analysis are more likely to be taken from patients that have developed complications or are suffering from co-morbidities, making it difficult to discover the true epidemiology of UTIs.

Six studies included both genders (Ruben *et al.* 1995, Ki *et al.* 2004, Galatti *et al.* 2006, Czaja *et al.* 2007, Laupland *et al.* 2007, Caljouw *et al.* 2011), of which one concluded that UTIs were significantly higher in females than males. Conversely, another found that UTI prevalence was higher in males than females (Omoregie *et al.* 2010). Several studies linked increased UTI incidence or prevalence with advancing age in all age groups

(Ruben *et al*. 1995, Malmsten *et al.* 1997, Molander *et al*. 2000, Galatti *et al*. 2006, Czaja *et al.* 2007, Eriksson *et al.* 2010, Marques *et al.* 2012). This could be owing to elderly weak immunity, the presence of co-morbidities, recurrent UTI infections, urinary tract system surgery, and impaired functional and cognitive status (Caljouw *et al.* 2011). That said, one study found that UTIs do not increase with age in females (Foxman *et al.* 2000) and another concluded that UTI prevalence decreased with advancing age (Omoregie *et al.* 2010).

Table 14: Summary of epidemiological studies of UTIs in elderly patients

| Author | Country | Study Design | Data Source | Measured Rate | N* | Results |
|---|---|---|---|---|---|---|
| Ruben *et al.* 1995 | USA | Prospective, observational | Visit and phone screening | Incidence | 417 | Overall: 13 per 100 persons per year<br>Female: 14 per 100 persons per year<br>Male 10.9 per 100 persons per year |
| Malmsten *et al.* 1997 | Sweden | Cohort | Postal questionnaire in male | Prevalence | 4,661 | 65: 6.4%<br>70: 4.5%<br>75: 8%<br>70: 10.7%<br>85-89: 13.9%<br>≥ 90: 16.5% |
| Molander *et al.* 2000 | Sweden | Cohort | Questionnaire in female | Prevalence | 4,206 | 1986: 16.36%<br>1995: 61% |
| Foxman *et al.* 2000 | USA | Prospective | Random phone numbers dialling survey in female | Incidence | 2,000 | Pyelonephritis: 9% |
| Ki *et al.* 2004 | South Korea | Retrospective | Insurance claims database | Incidence | N/A | Female cystitis (per 10,000):<br>60-79: 57.15<br>≥ 80: 28.07<br>Male cystitis (per 10,000):<br>60-79: 20.51<br>≥ 80: 25.10 |
| Galatti *et al.* 2006 | Italy | Retrospective | Health Search Database | Prevalence | 11,013 | Acute complicated cystitis: 50.1%<br>Recurrent cystitis: 53.2% |
| Czaja *et al.* 2007 | USA | Population-based, retrospective | Health Maintenance Organisation database | Incidence | N/A | Female pyelonephritis (per 10,000 person-years):<br>65-69: 9<br>70-74: 11<br>75-79: 12<br>80-84: 13<br>≥ 85: 12<br>Male pyelonephritis (per 10,000 person-years):<br>65-69: 5<br>70-74: 6<br>75-79: 7<br>80-84: 5<br>≥ 85: 6 |

Continued Table 14

| Author | Country | Study Design | Data Source | Measured Rate | N* | Results |
|---|---|---|---|---|---|---|
| Laupland *et al.* 2007 | Canada | Population-based, retrospective | Microbiology laboratory surveillance database | Incidence | N/A | Female (per 1,000 per year):<br>69-69: 40.<br>70-79: 46<br>80-89: 110<br>-Male:<br>69-69: 10<br>70-79: 15<br>80-89: 60 |
| Eriksson *et al.* 2010 | Sweden and Finland | Population-based, retrospective, cross-sectional | Home visits and medical records review in female | Prevalence | 395 | 85: 25%.<br>90: 29.6%.<br>95: 34.4%. |
| Omoregie *et al.* 2010 | Nigeria | Prospective | MSU urine analysis | Prevalence | 943 | Overall: 11.03%.<br>60−69: 14.46%.<br>70−79: 10.94%.<br>80−89: 8.26%.<br>90−99: 3.2%. |
| Caljouw *et al.* 2011 | Netherlands | Population-based, prospective, follow-up | Medical records and interviews | Incidence | 479 | 11.2 per 100 person-years. |
| Marques *et al.* 2012 | Brazil | Population-based, prospective | Medical records and MSU in female | Prevalence | 598 | 16.55%. |

* N: Number of elderly patients within study sample size N/A: Not available MSU Midstream urine

### 2.7.2 Antibiotics Prescribing and Appropriateness for Elderly Patients with UTIs

It has been reported that antibiotics utilisation research in community settings is not as well established as it is in inpatient settings (Carrie and Zhanel 1999, Carrie *et al.* 2000). In-depth research on antibiotics prescribing for elderly population in primary care setting was reported to be scarce (Haeseker *et al.* 2012). Antibiotics gained special attention over several drugs classes to reduce their unnecessary and inappropriate use, slowing the spread of AMR as well as cutting down associated costs (Hasan *et al.* 1997). Excessive antibiotics use by GPs can lead to unnecessary ADRs, encouraging patients to re-consult their GPs for subsequent similar problems, possible development of resistance and unnecessary utilisation for healthcare resources as well as services (Ong *et al.* 2008).

A number of studies revealed that antibiotics are one of the most commonly prescribed classes of drugs for elderly people (Norris *et al.* 2011, Pan *et al.* 2011, Haeseker *et al.* 2012). One study observed the highest use of antibiotics in elderly people aged 80 or older with 26 DDD/1,000 inhabitants per day followed by patients between the ages of 60 and 79 with 21 DDD/1,000 inhabitants per day (Pan *et al.* 2011).

In New Zealand, Norris *et al.* (2011) explored antibiotics use according to age, gender, ethnicity, socio-economic status and rurality using dispensed prescriptions electronic data from community pharmacies from 1 October 2005 to 30 September 2006. Findings showed a high prevalence of antibiotics prescribing among elderly individuals with an annual prevalence of 49% for those aged 65–74, 56% for those aged 75–84 and 69% for those aged 85 and over, making this prevalence the highest compared with middle-aged people and children. Similarly, the amount of prescribed antibiotics expressed in DDD per person per year broadly mimicked this pattern with 13.07 DDD per person per year for those aged 65–74, 14.68 DDD per person per year for those aged 75–84 and 19.03 DDD per person per year for those aged 85 and over making them again the highest compared with other age groups.

Haeseker *et al.*'s (2012) retrospective cohort analysis used the Dutch Registratie Netwerk Huisartsen (RNH) GP database to estimate the prescribing of different antibiotic classes among different age groups in Netherlands general practice from 2000 to 2009. The study included 65,894 patient years aged over 18. Elderly patients represented 21% (N = 140,999) of the total patient years, of which 16% (N=108,131) were aged 65–79 and 5%

(N = 32,868) were aged 80 or older. The highest increase in antibiotics prescribing was reported in elderly patients: 9% in 2000 rising to 22% in 2009 as a result of an increased number of RTI and UTI general practice consultations. The total number of patient years for elderly patients aged 65–79 who received at least one antibiotic was 15,440 (20%) and for those aged 80 or older the number was 5,478 (7%). Additionally, antibiotics were frequently prescribed in the elderly with significant association between age and antibiotics prescribing across all years ($p < 0.001$). The rate of antibiotics prescribing in elderly patients significantly increased over time with the highest increase in elderly patients aged 80 or older ($p < 0.001$). Two or more antibiotics per year were prescribed most often in elderly patients with 23% (N = 3,581) aged 65–79 and 29% (N = 1571) aged 80 or older. This increase in the number of antibiotics with age was found to be statistically significant ($p < 0.001$) with an independent increase over time and age.

In the UK, a medical database analysis of 179 GP surgeries showed that UTIs were found to be the fourth leading indication for antibiotic prescribing by (N = 44,826; 10%) in 2000–2001 after upper RTIs, lower RTIs and sore throat (Petersen and Hayward 2007a). UK GPs write about 5.5 million prescriptions for UTI treatment each year. A substantial number of these are for treating UTIs in the elderly (N = 1,595,000; 29%), of which 68.96% (N = 1,100,000) are for female patients (Reeves 1994). This frequency of prescribing as well as the substantial and serious consequences for patients, particularly elderly individuals, the healthcare system and society mean that attention must be paid to the utilisation and appropriateness of antibiotics for elderly patients (Leistevuo *et al.* 1997). The earlier literature review identified 12 studies on GPs' antibiotics prescribing and appropriateness for UTIs in elderly patients that were reviewed and critiqued in the following paragraphs. Table 15 summarises reviewed studies relevant to antibiotics prescribing for elderly patients with UTIs and GPs' adherence to UTI guidelines.

Friis *et al.* (1989) studied five of Denmark's 13 counties to explore Danish GPs' uses and choices of antibiotics for all ages. They recruited 1,012 GPs to collect data on patients, diagnosis and antibiotics used from 23 March 1987 to 27 March 1987. Results revealed that 60% (N = 602) of GPs prescribed antibiotics for 7,607 patients, of whom 12.69% (N = 966) were aged 65 or older. UTIs were the fourth most common infection diagnosed (N = 819; 10.76%) and were the most common cause for antibiotics treatment in the elderly (N = 290; 30%). Sulphamethizole was the most commonly prescribed antibiotic for UTIs (N = 451; 59%) with an average duration of 6.2 days, followed by ampicillin (N = 150;

20%) with an average duration of 6.8 days then TMP-SMX (N = 28; 4%) with an average duration of 11.5 days. The study had some significant limitations, though. First was the inappropriate use of DDD for children patients since this unit is appropriate only for adult measures. Second, no age–sex adjustment for rates of infections was performed; some infections are common at specific ages and in specific genders. Third, the study did not consider confounders such as seasonality in reporting certain infections such as RTIs. Fourth, no standard diagnostic criteria were used to eliminate the variation factor in diagnosis by different GPs, which could influence prescribing. Finally, the population from Denmark was relatively small and therefore not representative of other countries.

Leistevuo *et al.* (1997) conducted a retrospective study in Finland to describe the frequency of antibiotics prescribing for elderly people as well as identifying physician prescribing practice in Lieto's municipal healthcare centre, a mixed setting facility where the majority of working physicians were GPs for the period 1990–1991. The study included 1,196 elderly patients, representing 94% (N = 1,208) of Lieto's municipal elderly population. Of these, 41% (N = 488) were male and 59% (N = 708) were female. Also, 62% (N = 739) were aged 64–74, 31% (N = 374) were aged 75–84 and 7% (N = 83) were aged 85 or older. Non-institutionalised patients were higher in both genders and represented 94% (N = 662) of female patients and 96% (N = 469) of male patients. Before the researchers examined the patients, they retrieved the preceding year's data for patients' antibiotics prescriptions from patients' medical records. The findings showed that 27.1% (N = 127) of non-institutionalised male patients and 33.1% (N = 219) of non-institutionalised female patients were prescribed at least one antibiotic in the preceding year. UTI was the most common type of infection for antibiotics prescribing in both genders. Female patients received more antibiotics prescriptions for UTIs (N = 153; 60%) than male patients (N = 25; 18%). Of the non-institutionalised female patients with UTIs, 58% (N = 74) received antibiotic therapy, whereas 10% (N = 13) of non-institutionalised male patients did. Most male patients with UTIs were prescribed first generation cephalosporins (N = 50; 36%), TMP-SMX or trimethoprim alone (N = 43; 31%) and quinolones (N = 17; 12%). Female patients were prescribed TMP-SMX or trimethoprim alone (N = 94; 37%), pivmecillinam (N = 61; 24%) and first-generation cephalosporins (N = 56; 22%). Interestingly, although the findings were in line with national figures for Finland, there were limitations to the study. First, it failed to distinguish between institutionalised and non-institutionalised patients in terms of antibiotics prescribed for UTIs for each gender. Second, it could not compare the findings with any similar studies especially in non-institutionalised patients. Third, the population from Finland was relatively small and therefore not representative of other countries.

In one Norwegian county, Straand *et al.* (1998) performed a prospective, cross-sectional, observational study of GPs' prescribing patterns for antibiotics with regard to type, quantity, patients' ages and genders compared with guidelines for November 1988 to November 1989. Data were collected by 149 GPs who represented 96% of the county's total GPs. The GPs issued 56,758 prescriptions, of which 14% (N = 7,905) were for systemic antibiotics. In total, 1,649 (22.26%) prescriptions were issued for elderly patients aged 60 and older. Of these, 1,097 (14.81%) were for females and 552 (7.45%) were for males. Tetracyclines (N = 166; 30.07%) followed by TMP-SMX (N = 142; 25.72%) were the most commonly prescribed antibiotics for male elderly patients. In females, TMP-SMX (N = 323; 29.44%) was followed by tetracyclines (N = 181; 16.49%). In general, UTIs were the most common cause of antibiotics prescribing (N = 1,871; 23.66%), for which TMP-SMX was the most commonly prescribed drug (N = 844; 45.1%) followed by trimethoprim (N = 365; 19.5%) then extended spectrum penicillins (N = 344; 18.4%). GPs did not prescribe according to UTI guidelines since almost half of all UTI prescriptions were co-trimoxazole when the recommendations suggest using trimethoprim and sulphonamides as first-line antibiotics for UTIs. One significant limitation of the study related to antibiotics prescriptions issued through indirect contact, whether by telephone, letter or a third person, which can result in either over-prescribing or under-prescribing in certain infections such as UTIs that require laboratory test and microbiology to confirm diagnosis, especially in elderly patients with atypical presentations.

In the UK, Wrigley *et al.*'s (2002) retrospective analysis examined GPs' antibiotics prescribing trends and investigated the influence of published guidelines and literature on GPs' prescribing practice in England and Wales from 1994 to 1998. Data were retrieved from the General Practice Research Database (GPRD) and included patients' medical information from 210 general practices, among which 843,767 systemic antibiotics prescriptions were found. Findings showed that elderly patients had the second highest exposure to antibiotics after children under five years, with antibiotics prescriptions numbering 712 (31.1%) in males and 852 (36.1%) in females aged 65–74, 854 (34.5%) in males and 914 (37%) in females aged 75–84 and 1,007 (37%) in males and 1,042 (40%) in females aged 85 years or older. Moreover, the analysis showed a marked variation in the use of sulphonamides, cephalosporins, broad-spectrum penicillins and trimethoprim, which was justified by the difference in the use of these antibiotics for the treatment of UTIs. The study, however, failed to measure GPs' adherence to UTI recommendations, owing to a lack of prescription duration information, or to distinguish between antibiotics prescribed and those dispensed, since the numbers included delayed prescriptions, meaning that an overestimation of antibiotics prescriptions cannot be ruled out. Additionally, there was no data linking between prescriptions, which could have provided useful information about the trend of antibiotics prescribing for specific types of infection.

Kahan *et al.* (2005) carried out retrospective data analysis on computerised medical records to evaluate physicians' adherence to recommendations for the empiric treatment of uncomplicated UTIs in adult female patients in a community setting in Israel between July 2000 and June 2002. Retrieved data included visit date, patient and physician identification numbers, diagnosis code, drug prescribed and referrals. In this study, which identified 64,236 cases of uncomplicated UTI, guidelines recommended the use of nitrofurantoin and TMP-SMX as first-line drugs. Results showed that only 35.55% (N = 22,833) of cases received antibiotics that were in line with recommendations. TMP-SMX and nitrofurantoin were prescribed in 17.04% (N = 10,945) and 18.51% (N = 11,888) of all cases respectively. Although not recommended, fluoroquinolones were the most commonly prescribed antibiotics in 25.57% (N = 16,428) of cases, with 52.01% (N = 5,692) ofloxacin, 47.71% (N = 5,222) ciprofloxacin and 0.28% (N = 31) levofloxacin and norfloxacin. The study concluded that adherence to guidelines among community-setting physicians was poor. This study had limitations such as imprecise use of the disease classification system, disease misclassification and incomplete capture of all cases. Additionally, the study lacked patients' clinical information, culture results and laboratory results, which could have influenced physicians' antibiotic choices.

Retrospective data analysis was performed in the UK by the Specialist Advisory Committee on Antibiotic Resistance (SACAR) to explore antibiotics prescribing in primary care settings and the usefulness of GPRD as a database for antibiotics surveillance between 1998 and 2001. Of 53,748 patients with UTIs, only 83.4% (N = 44,826) received antibiotics: trimethoprim (N = 25,147; 56.1%), cephalexin (N = 6,365; 14.2%), amoxicillin (N = 2,779; 6.2%), nitrofurantoin (N = 2,286; 5.1%), ciprofloxacin (N = 1,838; 4.1%), co-amoxiclav (N = 1,748; 3.9%), cefradine (N = 1,614; 3.6%), cefadroxil (N = 941; 2.1%), norfloxacin (N = 807; 1.8%), cefaclor (N = 493; 1.1%) and others (N = 807; 1.8%). Although the study demonstrated GPRD's usefulness as a database for monitoring antibiotics, it was limited by under-recording of UTIs by some GPs who tended to record only major infections during consultations, which may have resulted in prescriptions overestimation for these infections compared with the minor infections. Another limitation related to the lack of distinguishing between antibiotics prescribed and those dispensed, since the numbers included delayed prescriptions, meaning that an overestimation of antibiotics prescriptions cannot be ruled out. The study also reported that prescribing in primary care was most often in line with current recommendations without reporting any results or details about GPs' adherence (Petersen and Hayward 2007a).

In the USA, retrospective, cross-sectional analysis of data retrieved from an ambulatory medical services database[18] between 1996 and 2001 examined prescribing practices for treating uncomplicated UTIs in females aged 18 or older and the influence of the IDSA 1999 guidelines. The study identified 2,339 uncomplicated UTI cases, which was projected to be 41.6 million patient visits (95% CI 37.9–45.4) to a healthcare provider in the USA during the study period with an average of almost 7 million patient visits per year. Of these cases, 24.48% (N = 582) were patients aged 60–79 with weighted visits of 27.8% (95% CI 25.7–32.9) and 8.46% (N = 198) were patients aged 80 or older with weighted visits of 9.5% (95% CI 7.1–11.9). The most commonly prescribed antibiotics were TMP-SMX in 26.5% (N = 620) of visits with weighted visits of 29.8% (95% CI 25.9–33.7), ciprofloxacin in 14.02% (N = 328) of visits with weighted visits of 24.2% (95% CI 20.1–28.4), nitrofurantoin in 11.07% (N = 259) of visits with weighted visits of 18.8% (95% CI 15.0–22.6), fluoroquinolones excluding ciprofloxacin in 5.55% (N = 130) of visits with weighted visits of 11.2% (95% CI 8.6–13.8) and amoxicillin in 2.09% (N = 49) of visits with weighted visits of 2.6 % (95% CI 1.3–3.8). Use of ciprofloxacin increased since the introduction of the IDSA guidelines by approximately two-thirds (OR 1.75; 95% CI 1.11–2.75) and ($p$ = 0.016) whereas the use of other antibiotics did not significantly change, which made ciprofloxacin the preferred drug. Overuse of fluoroquinolones made TMP-SMX, which was the recommended antibiotic for uncomplicated UTIs, not the drug of choice. The study confirmed that primary care physicians generally lack adherence to IDSA guidelines. However, it had limitations

[18] A database that included non-federally employed patients visiting primary care.

related to UTI misclassification and the possibility of treating other UTI classes as uncomplicated UTIs. Additionally, some cases were given antibiotics based on microbial culture results making the decision in these cases more directed than empirical (Taur and Smith 2007).

McIsaac *et al.* (2008) performed a retrospective, cross-sectional study to determine Canadian primary care physicians' first-line antibiotics choices for treating adult female patients with symptoms suggestive of acute cystitis between April 2002 and March 2003. The study recruited 418 full-time family physicians who detected 446 cases of cystitis in female patients, of whom 79 (17.7%) were elderly, aged 65–99. The results revealed that 86.9% (N = 365) of female patients with suggestive cystitis received an antibiotic prescription (95% CI 83.3–90.0). Urine culture testing was requested for 311 of the 365 patients with antibiotic prescriptions, with culture results returned negative in 102 cases (32.8%). In other words, 32.8% of female patients received unnecessary antibiotic therapy. TMP-SMX was the most commonly prescribed first-line antibiotic drug (N = 149; 40.8%) (95% CI 35.7–46.1). Most TMP-SMX treated patients received a prescription for a course of seven or more days (N = 55; 36.9%), followed by three days (N = 54; 36.2%) then five days (N = 40; 26.8%). The mean duration of antibiotic therapy in elderly females was 5.4 days, which was not shown to be significant if compared with young females ($p = 0.39$). Fluoroquinolones were the second most commonly prescribed empirical antibiotics after TMP-SMX in 27.4% (N = 100) of cases (95% CI 22.9–32.3). Patients who received fluoroquinolones used them for durations of three days in 37.4% of cases (N = 37/99), five days in 29.3% of cases (N = 29/99) and seven or more days in 33.3% of cases (N = 33/99). Females aged 65 or older were prescribed fluoroquinolones as a second-line empirical therapy (N = 21/65; 32.3%) with no statistical difference compared with young females ($p = 0.50$). Nitrofurantoin was the third most commonly prescribed antibiotic in 26.6% (N = 97) of cases (95% CI 22.1–31.4). The majority of patients were prescribed nitrofurantoin for the recommended seven days (N = 52/97; 53.6%), although 46.4% (N = 45/97) were prescribed for fewer days. A three-day course was prescribed in 19.6% (N =19) of cases. There was no difference in nitrofurantoin use among all age groups ($p = 0.56$). The study concluded that prescribing in Canada was associated with a high level of unnecessary antibiotics use and physicians had a habit of prescribing fluoroquinolones more frequently, which can lead to increased fluoroquinolones bacterial resistance. One of its limitations was the use of old collected data to measure adherence levels with an updated recommendation, as the prescribing at that time would not have been a fair representation of current antibiotics prescribing practice. Additionally, the results from this study might not represent family physicians' antibiotics prescribing practice in Canada since the participating number of family physicians was small compared with the total number of physicians contacted, which was 2,000.

In Ireland, a prospective study evaluated the management and appropriateness of GPs' antibiotics therapy for UTIs in adult patients including the elderly in relation to urine sample laboratory results from 14 September 2009 to 9 November 2009. The study examined urine samples from 866 patients from 22 GP surgeries using microscopy and semi-quantitative culture testing. The culture was positive in 21% (N = 183) of patients, 8.8% (N = 76) of patients had pyuria and there was no evidence of UTI in 70.1% (N = 607) of patients. In total, 56% (N = 481) of patients received an antibiotics prescription, of whom 55.7% (N = 268) had no laboratory evidence of UTIs and 37.2% (N = 179) received first-line antibiotics (nitrofurantoin or trimethoprim). Co-amoxiclav was the most commonly prescribed antibiotic, prescribed to 159 patients (33.1%), of whom 87 (54.7%) had no laboratory evidence of UTI; followed by trimethoprim, prescribed to 126 patients (26%), of whom 60 (48%) had no laboratory evidence of UTI; then fluoroquinolone, prescribed to 82 patients (17%), of whom 54 (65.9%) had no laboratory evidence of UTI; and nitrofurantoin, prescribed to 57 patients (11.9%), of whom 29 (50.9%) had no laboratory evidence of UTI. Empirical antibiotics therapy appropriateness was evaluated based on three simulated scenarios that showed general antibiotics prescribing was appropriate in 55.2% of cases (N = 478), with 57.5% (N = 498) for nitrofurantoin, 52.5% (N = 455) for trimethoprim and 57.6% (N = 499) for fluoroquinolones. Overall, 55% of the patients received appropriate antibiotics treatment for uncomplicated UTIs. However, the study had limitations in terms of categorisation of appropriateness of empirical UTI therapy, which was based on non-validated simulated scenarios against the first-line therapy recommended in the guidelines. Additionally, the use of pyuria as an indicator for UTI was not reliable since pyuria can be associated with other conditions (Vellinga *et al.* 2011).

Llor *et al.* (2011) conducted a cross-sectional study to determine Spanish GPs' adherence to diagnostic and therapeutic guidelines for LUTIs in females using a data registry to collect clinical data between March 2009 and July 2009. The registry data were completed by 176 GPs who identified 658 females with LUTIs. Results revealed that antibiotics were prescribed in 634 (96.4%) cases, of whom 545 (82.82%) had uncomplicated UTIs and 113 (17.17%) had complicated UTIs. Antibiotics were prescribed for all complicated cases but only 521 (95.59%) uncomplicated cases. First-line drug therapy was prescribed to 111 (17.5%) females, of whom 92 (16.88%) had uncomplicated UTIs and 19 (16.81%) had complicated UTIs. Fosfomycin was the most often prescribed antibiotic for UTIs in 299 (47.16%) cases with the majority receiving a prescription for a two-day course (N = 241; 80.60%) and 19.39% (N = 58) receiving a prescription for a single dose. Co-amoxiclav was the second most commonly prescribed antibiotic in 97 (15.29%) cases with the majority receiving a prescription for a seven-day course (N = 75; 77.31%) and 22.68% (N = 22) receiving a prescription for a five-day course. Fluoroquinolones were the third most commonly prescribed antibiotics in 75 (11.82%) cases, who received norfloxacin mainly for seven days (N = 51; 68%) followed by three days (N = 18; 24%) then five days (N = 6; 8%); ciprofloxacin was also prescribed in 63 (9.93%) cases for seven days (N = 36; 57.14%) and five days (N = 26; 41.26%). Overall, prescribing short antibiotics courses was preferred by 60.7% (N = 385) of GPs; however, short duration courses were prescribed more often in uncomplicated UTI cases (N = 347; 66.6%) compared with (N = 174; 33.4%) longer courses, whereas longer duration courses were more often used in complicated UTI cases (N = 75; 66.4%) compared with (N = 38; 33.6%) shorter courses. Spanish GPs had poor adherence to guideline recommendations with low utilisation of first-line antibiotics. The study was limited by the small number of recruited GPs, and by failing to link the results of antibiotics duration with the complicatedness of UTI cases. Also, performing an audit study may influence GPs' prescribing habits by exposing them to the Hawthorne effect.[19] Finally, the study was sponsored by a pharmaceutical company, which could have resulted in biased findings.

In France, a prospective study evaluated whether French GPs adhere to the 2008 UTI guidelines by comparing urine analysis results with prescribed antibiotics during September 2010. The study included 185 urinalyses samples requested by 122 GPs. The results showed that only 20% (N = 37) of patients received antibiotics prescriptions that were in line with the recommendations. Moreover, 71.35% (N = 132) of patients received an antibiotic that was not recommended as a first-line drug, including 70.1% (N = 94) of all cystitis cases. Although antibiotics prescribing was in line with recommendations in 8.64% (N = 16) of patients, these patients received a prescription with either an incorrect

[19] Where a study subject's behaviour and/or the study outcomes are altered as a result of the subject's awareness of being under observation (Mangione-Smith *et al.* 2002, p. 1604).

dose and/or an incorrect treatment duration. Ciprofloxacin and nitrofurantoin were mostly associated with dose error, with GPs prescribing only 50% of the recommended dose, whereas short courses for prostatitis and long courses for cystitis were the two main problems associated with incorrect antibiotics duration. Furthermore, GPs prescribed fluoroquinolones in 59.49% (N = 110) of all UTI cases, of which 77.27% (N = 85) were not in line with recommendations. The majority of cystitis patients were treated with fluoroquinolones then nitrofurantoin. The study concluded that GPs were not following the guidelines sufficiently and that the majority of UTIs were being treated inappropriately with fluoroquinolones. One of its limitations related to the process of treating patients with cystitis without the use of urinalyses, which might result in UTI population misrepresentation. Another was that the treatment comparison with the guidelines was based on diagnoses established by the GPs, which could have deviated from the recommendations according to the patients' condition. Additionally, the accuracy of the GPs' diagnoses was not established, which could result in the wrong antibiotic being selected for the wrong condition, which was consequently considered as a deviation from the guidelines. Moreover, the data from this study were presented in the form of graphs only, which made the results difficult to interpret especially in terms of data comparisons (Denes *et al.* 2012).

Haasum *et al.* (2013) conducted a retrospective, cross-sectional analysis of the Swedish Prescribed Drug Register (SPDR) to compare the quality of antibiotic drugs use for treating UTIs in home-dwelling and institutionalised elderly patients against Swedish and European guidelines. The study included dispensed drugs data for people aged 65 and older from 1 July 2008 to 30 September 2008. Of the 12,455 elderly males and females who used antibiotics for UTIs during the study period, the calculated prevalence was 1.6% (N = 1,392/86,721) for institutionalised elderly compared with 0.9% (N = 11,063/1,260,843) in the community. Among home-dwelling female UTI patients aged 65–79, pivmecillinam (N = 1,457; 32.1%), trimethoprim (N = 1,210; 26.7%), nitrofurantoin (N = 1,077; 23.8%) and quinolones (N = 955; 21.1%) were the most commonly used antibiotics; while for those aged 80 or older the most commonly used antibiotics were pivmecillinam (N = 1,022; 34.6%), trimethoprim (N = 882; 29.8%), nitrofurantoin (N= 678; 22.9%) and quinolones (N = 460; 15.6%). For home-dwelling male UTI patients aged 65–79, the most commonly used antibiotics were quinolones (N = 1,584; 68.2%), trimethoprim (N = 432; 18.6%), nitrofurantoin (N = 208; 9.0%) and pivmecillinam (N = 157; 6.8%); while for those aged 80 or older the most commonly used antibiotics were quinolones (N = 726; 58.1%), trimethoprim (N = 327; 26.2%), pivmecillinam (N = 115; 9.2%) and nitrofurantoin (N = 108; 8.6%). GPs poorly adhered to the recommendations in both settings. However, use of pivmecillinam for UTIs might reflect the proper implementation of guidelines in females. Quinolones were used more frequently than advised in both settings and nitrofurantoin was used to a lesser extent in females than was recommended. In males, the use of quinolones and trimethoprim was in line with recommendations in both settings. Conversely, use of nitrofurantoin in males was higher than recommended, especially in elderly patients aged 80 or older. However, the lack of patients' clinical information, the lack of laboratory results for renal function, urinalysis and cultures, the lack of the reason for antibiotics prescribing for treatment or prophylaxis, the lack of linking between prescribed antibiotics and those dispensed as well as the lack of distinguishing between ASB and UTIs were all significant limitations of this study.

In conclusion, there were 12 studies describing the appropriateness of GPs prescribing antibiotics for UTIs. Two were from the UK (Wrigley *et al.* 2002, Petersen and Hayward 2007a), seven were from other European countries, namely, Denmark, Finland, Norway, Ireland, Spain, France and Sweden (Friis *et al.* 1989, Leistevuo *et al.* 1997, Straand *et al.* 1998, Llor *et al.* 2011, Vellinga *et al.* 2011, Denes *et al.* 2012, Haasum *et al.* 2013), one was from the USA (Taur and Smith 2007), one from Canada (McIsaac *et al.* 2008) and one from Israel (Kahan *et al.* 2005). Eight studies evaluated primary care GPs', doctors' or physicians' adherence to UTI guidelines (Straand *et al.* 1998, Kahan *et al.* 2005, Taur and Smith 2007, McIsaac *et al.* 2008, Llor *et al.* 2011, Vellinga *et al.* 2011, Denes *et al.* 2012, Haasum *et al.* 2013). Two studies were designed specifically for the elderly population (Leistevuo *et al.* 1997, Haasum *et al.* 2013) and the rest included elderly people as part of the studied population, of which six clearly stated the number of elderly patients included (Friis *et al.* 1989, Straand *et al.* 1998, Wrigley *et al.* 2002, Taur and Smith 2007, McIsaac *et al.* 2008, Haasum *et al.* 2013). Three studies covered antibiotics prescribing for female patients with UTIs in general including elderly people (Kahan *et al.* 2005, McIsaac *et al.* 2008, Llor *et al.* 2011). Additionally, the studies varied in research design and data sources, ranging from manual data collection in three studies (Friis *et al.* 1989, Leistevuo *et al.* 1997, Llor *et al.* 2011), databases in five (Wrigley *et al.* 2002, Kahan *et al.* 2005, Petersen and Hayward 2007a, Taur and Smith 2007, Haasum *et al.* 2013) and urine culture results in three (McIsaac *et al.* 2008, Vellinga *et al.* 2011, Denes *et al.* 2012).

Each study on antibiotics prescribing for UTIs in the community setting is unique in its methodological approach and presentation of results. This makes it challenging to draw direct comparisons about how and why antibiotics are prescribed for UTIs. Studies from different countries adopted different guidelines to audit the appropriateness of different first-line antibiotics. Moreover, first-line treatment recommendations might differ within the same country as bacteria develop resistance over time. GPs might deviate from prescribing guidelines when urine sample results show resistance bacteria, or when the patient has a reason that makes first-line therapy inappropriate, such as drug–drug interactions or ADRs. Nonetheless, some notable trends were apparent. Elderly females received more antibiotic prescriptions for UTIs than elderly males (Leistevuo *et al.* 1997). 'Poor' or 'lacking' were the two words used to describe GPs' adherence to UTI guidelines in all studies designed to evaluate GPs' prescribing practice (Straand *et al.* 1998, Kahan *et al.* 2005, Taur and Smith 2007, McIsaac *et al.* 2008, Llor *et al.* 2011, Vellinga *et al.* 2011, Denes *et al.* 2012, Haasum *et al.* 2013). Additionally, there was notably increased prescribing of fluoroquinolones for UTIs in six studies (Kahan *et al.* 2005, Taur and Smith 2007, McIsaac *et al.* 2008, Llor *et al.* 2011, Vellinga *et al.* 2011, Denes *et al.* 2012), although these are not recommended. This trend could have disastrous consequences for the growing bacterial resistance problem. Furthermore, TMP-SMX or trimethoprim appear to be the most frequently prescribed antibiotics by for UTIs (Leistevuo *et al.* 1997, Straand *et al.* 1998, Kahan *et al.* 2005, Petersen and Hayward 2007a, Taur and Smith 2007, McIsaac *et al.* 2008). Critical appraisal of the studies that used urine samples suggested that some GPs are more likely to send samples for microbiological analysis than others, for instance, if they have a low tendency to prescribe antibiotics (McIsaac *et al.* 2008, Vellinga *et al.* 2011, Denes *et al.* 2012).

Table 15: Summary of studies relevant to antibiotics prescribing for elderly patients with UTIs and GPs' adherence to UTI guidelines

| Author | Country | Study Design | Data Source | N* | Results |
|---|---|---|---|---|---|
| Friis *et al.* 1989 | Denmark | Prospective | Data collection chart | 966 EPats | -UTIs were the most common cause for antibiotic treatment in elderly (N = 290; 30%)<br>-Frequently prescribed antibiotics for UTIs were:<br>Sulphamethizole: (N = 451; 59%) average duration of 6.2 days<br>Ampicillin: (150; 20%) average duration of 6.8 days<br>TMP-SMX: (N = 28; 4%) average duration of 11.5 days |
| Leistevuo *et al.* 1997 | Finland | Retrospective | GPs' records | 1,196 EPats | -UTIs were the most common infection for antibiotic prescribing.<br>-Female received more antibiotic prescriptions (N = 153; 60%)<br>-Non-institutionalised female patients with UTIs received more antibiotic therapy (N = 74; 58%)<br>-Frequently prescribed antibiotics for UTIs in male:<br>1st generation cephalosporins: (N = 50; 36%)<br>TMP-SMX or trimethoprim alone: (N = 43; 31%)<br>Quinolones: (N = 17; 12%)<br>-Frequently prescribed antibiotics for UTIs in female:<br>TMP-SMX or trimethoprim alone: (N = 94; 37%)<br>Pivmecillinam: (N = 61; 24%)<br>1st generation cephalosporins: (N = 56; 22%) |
| Straand *et al.* 1998 | Norway | Prospective cross-sectional | GPs collected antibiotic prescriptions | 1,649 EPres | -UTIs were the most common cause of antibiotics prescribing in (N = 1871; 23.66%)<br>-Frequently prescribed antibiotics for UTIs were:<br>Co-trimoxazole: (N =844; 45.1%)<br>Trimethoprim: (N = 365; 19.5%)<br>Extended spectrum penicillins: (N = 344; 18.4%)<br>-GPs did not prescribe antibiotic for UTIs according to guideline recommendations |
| Wrigley *et al.* 2002 | UK | Retrospective analysis | GPRD | 5,381 EPres | -Marked variation in the use of sulphonamides, cephalosporins, broad-spectrum penicillins and trimethoprim |
| Kahan *et al.* 2005 | Israel | Retrospective analysis | Computerised medical records | 64,236 cases | -TMP-SMX (N = 10,945; 17.04%)<br>-Nitrofurantoin (N = 11,888; 18.51%)<br>-Antibiotics were in line with guideline recommendation in (N = 22,833; 35.55%) cases<br>-Fluoroquinolones were not recommended by guideline and were prescribed in (N = 16,428; 25.57%)<br>-Adherence to guideline was found to be poor |

Continued Table 15

| Author | Country | Study Design | Data Source | N* | Results |
|---|---|---|---|---|---|
| Petersen and Hayward 2007 | UK | Retrospective data analysis | GPRD | 53,748 patients | - A total of (N = 44,826; 83.4%) patients received antibiotic for UTIs as follow:<br>Trimethoprim: (N = 25,147; 56.1%)<br>Cephalexin: (N = 6,365; 14.2%)<br>Amoxicillin: (N = 2,779; 6.2%)<br>Nitrofurantoin: (N = 2,286; 5.1%)<br>Ciprofloxacin: (N = 1,838; 4.1%)<br>Co-amoxiclav: (N = 1,748; 3.9%)<br>Cefradine: (N = 1,614; 3.6%)<br>Cefadroxil: (N = 941; 2.1%)<br>Norfloxacin: (N = 807; 1.8%)<br>Cefaclor: (N = 493; 1.1%)<br>Others: (N = 807; 1.8%) |
| Taur and Smith 2007 | USA | Retrospective, cross-sectional data analysis | Ambulatory medical services database | 780 EPats | -Prescriptions for uncomplicated UTIs were as follow:<br>TMP-SMX in (N = 620; 26.50%)<br>Ciprofloxacin in (N = 328; 14.02%)<br>Nitrofurantoin in (N = 259; 11.07%)<br>Fluoroquinolones other than ciprofloxacin in (N = 130; 5.55%)<br>Amoxicillin in (N = 49; 2.09%)<br>-There was increase in ciprofloxacin use by 2/3 ($p$ = 0.016)<br>-Primary care physicians generally lack adherence to guidelines |
| McIsaac *et al.* 2008 | Canada | Retrospective, cross-sectional | Primary care clinics visits and urine culture by adult female | 79 EPats | -Prescriptions for acute cystitis were as follow:<br>TMP-SMX (N = 149; 40.8%) (95% CI 35.7 - 46.1):<br>≥ 7-day (N = 55; 36.9%)<br>3-day (N = 54; 36.2%)<br>5-day course (40, 26.8%)<br>-Mean duration of therapy in elderly females 5.4 days ($p$=0.39) compared with young females<br>-Fluoroquinolones were the 2nd commonly prescribed empirical antibiotic in (N = 100; 27.4%) (95% CI 22.9 - 32.3)<br>-Fluoroquinolones were used for durations between 3 days in (N = 37/99; 37.4%), 5 days in (N = 29/99; 29.3%) and ≥ 7 days in (N = 33/99; 33.3%)<br>-Females 65 years or older were prescribed fluoroquinolones (2nd line) empirical therapy in (N =21/65; 32.3%) ($p$=0.50) compared with young females<br>-Nitrofurantoin was the 3rd commonly prescribed antibiotic in (N = 97; 26.6%) (95% CI 22.1- 31.4) patients<br>-Nitrofurantoin were prescribed for 7 days in (52/97, 53.6%) |

Continued Table 15

| Author | Country | Study Design | Data Source | N* | Results |
|---|---|---|---|---|---|
| McIsaac *et al.* 2008 | Canada | Retrospective, cross-sectional | Primary care clinics visits and urine culture by adult female | 79 EPats | -Nitrofurantoin were prescribed for 7 days in (52/97, 53.6%)<br>-Nitrofurantoin were prescribed for females less than the recommended 7 days duration in (N= 45/97; 46.4%)<br>-Three-days course was prescribed in (N =19; 19.6%) patients<br>-No statistical difference in the use of nitrofurantoin among all age groups ($p$=0.56)<br>-High level of unnecessary antibiotic use was reported<br>-Physicians had a habit to prescribe fluoroquinolones more frequently |
| Vellinga *et al.* 2011 | Ireland | Prospective | urine samples laboratory results | 866 patients | -A total of (N = 481; 56%) patients received antibiotic prescription (N = 268; 55.7%) with no laboratory evidence of UTIs<br>-First-line antibiotics (nitrofurantoin/trimethoprim) were received in (N = 179; 37.2%)<br>-Co-amoxiclav prescribed in (N = 159; 33.1%) patients, of whom (N = 87; 54.7%) with no laboratory evidence of UTIs<br>-Trimethoprim prescribed in (N = 126; 26%) patients, of whom (N = 60; 48%) with no laboratory evidence of UTIs<br>-Fluoroquinolones prescribed in (N = 82; 17%) patients, of whom (N = 54; 65.9%) prescriptions with no laboratory evidence of UTIs<br>-Nitrofurantoin prescribed in (N = 57; 11.9%) patients, of whom (N = 29; 50.9%) with no laboratory evidence of UTIs<br>-Empirical antibiotic simulation showed appropriateness of prescribing by GPs as follow:<br>General antibiotic prescribing: (N = 478; 55.2%)<br>Nitrofurantoin (N = 498; 57.5%)<br>Trimethoprim (N = 455; 52.5%)<br>Fluoroquinolones (N = 499; 57.6%)<br>-Overall, 55% of the patients received appropriate antibiotic treatment for uncomplicated UTIs |
| Llor *et al.* 2011 | Spain | Cross-sectional | Clinical data registry for LUTIs in females | 658 cases | Antibiotics were prescribed in (N = 634; 96.4%) cases, of whom (N = 545; 82.82%) uncomplicated UTIs and (N = 113; 17.17%) complicated UTIs<br>Antibiotics were prescribed for all complicated cases and only in (N = 521; 95.59%) cases of uncomplicated UTIs<br>-First-line antibiotic was prescribed in (N = 111; 17.5%) females, of whom (N = 92;17.7%) is uncomplicated UTIs and (N = 19; 16.8%) in complicated UTIs. |

Continued Table 15

| Author | Country | Study Design | Data Source | N* | Results |
|---|---|---|---|---|---|
| Llor *et al.* 2011 | Spain | Cross-sectional | Clinical data registry for LUTIs in females | 658 cases | -Fosfomycin was the most often prescribed antibiotic for UTIs in (N = 299; 47.16) cases with a majority of prescriptions for duration of 2 days (N = 241; 80.60%) whereas (N = 58; 19.39%) cases received a single dose prescription.<br>-Co-amoxiclav was the 2nd commonly prescribed antibiotic in (N = 97; 15.29%) cases with majority received a prescription for 7 days (N = 75;77.31%) and (N = 22;22.68%) for 5 days.<br>-Fluoroquinolones were the 3rd commonly prescribed antibiotics in (N = 75; 11.82%) cases<br>-Norfloxacin was prescribed for 7 days in (N = 51; 68%) followed by 3 days in (N = 18; 24%) and then 5 days in (N = 6; 8%)<br>-Ciprofloxacin was prescribed in (N = 63; 9.93%) for 7 days in (N = 36; 57.14%) and (N = 26; 41.26%) for 5 days<br>-Overall, prescribing short antibiotic courses were more preferred by (N = 385; 60.7%) GPs<br>-Short duration courses where more often in uncomplicated UTIs cases (N = 347; 66.6%) compared to (N = 174; 33.4%) longer courses<br>-Longer duration courses were more often in complicated UTIs cases (N = 75; 66.4%) compared to (N = 38; 33.6%) shorter courses.<br>-Spanish GPs had poor adherence to guidelines recommendation with a low utilisation of first-line antibiotic |
| Denes *et al.* 2012 | France | Prospective | Urine analyses results | 185 UAS | -Adherence to 1st line antibiotic choice was seen in (N = 37; 20%) patients<br>-Incorrect dose and/or duration of treatment was seen in (N = 16; 8.64%) patients<br>-A total of (N = 132; 71.35%) patients received an antibiotic which was not recommended as first-line drug, of which (N = 94; 70.1%) of all cystitis cases.<br>-Ciprofloxacin and nitrofurantoin were mostly associated with dose error by writing 50% of the recommended dose<br>-Short courses for prostatitis and long courses for cystitis were the main two problems associated with incorrect antibiotic duration<br>-GPs prescribed fluoroquinolones in (N = 110; 59.49%) of all UTIs cases, of which (N = 85; 77.27%) were not in line with guideline<br>-The majority of cystitis patients were treated with fluoroquinolones and then nitrofurantoin.<br>-GPs were not following the current guideline recommendations sufficiently<br>-Majority of UTIs treated with fluoroquinolones inappropriately |

Continued Table 15

| Author | Country | Study Design | Data Source | N* | Results |
|---|---|---|---|---|---|
| Haasum *et al.* 2013 | Sweden | Retrospective, cross-sectional data analysis | SPDR | 12,455 EPats | -Prevalence for elderly patients who received antibiotics for UTIs was (N = 1,392/86,721; 1.6 %) for institutionalised elderly compared to (11,063/1,260,843; 0.9 %) in the community.<br>-Frequently prescribed antibiotics in home-dwelling females aged 65 to 79:<br>Pivmecillinam (N = 1,457; 32.1%).<br>Trimethoprim (N = 1,210; 26.7%).<br>Nitrofurantoin (N = 1,077; 23.8%).<br>Quinolones (N = 955; 21.1%).<br>-Frequently prescribed antibiotics in home-dwelling females aged ≥80:<br>Pivmecillinam (N = 1,022;34.6%).<br>Trimethoprim (N = 882;29.8%).<br>Nitrofurantoin (N= 678;22.9%).<br>Quinolones (N = 460; 15.6%).<br>-Frequently prescribed antibiotics in home-dwelling males aged 65 to 79:<br>Quinolones (N = 1,584; 68.2%).<br>Trimethoprim (N = 432;18.6%).<br>Nitrofurantoin (N = 208; 9.0%).<br>Pivmecillinam (N = 157;6.8%).<br>-Frequently prescribed antibiotics in home-dwelling males aged ≥80:<br>Quinolones (N = 726;58.1%).<br>Trimethoprim (N = 327;26.2%).<br>Pivmecillinam (N = 115;9.2%).<br>Nitrofurantoin (N = 108;8.6%).<br>-GPs had poor adherence with recommendations in both settings.<br>-Use of pivmecillinam reflect the proper implementation of guideline in females.<br>-Quinolones were used more frequently than advised by guideline in both settings in females.<br>Nitrofurantoin was used in a lesser extent in females than the recommendations.<br>-Use of quinolones and trimethoprim were in line with guideline in both settings in males.<br>-Use of nitrofurantoin was higher than the recommended in males especially those aged 80 years or older. |

* N: refers to number of elderly patients participated in the study or number for prescriptions for elderly patients) TMP-SMX: Trimethoprim-Sulfamethoxozole EPats: elderly patients EPres: elderly prescriptions UAS: urinalyses samples; SPDR: Swedish Prescribed Drug Register; GPRD: General Practice Research Database

### 2.7.3 Variations in GPs' Views and Perceptions of Antibiotics Prescribing for UTIs for Elderly Patients in a Primary Care Setting

Considerable works of qualitative research have contributed to the current knowledge related to understanding the cultures, views and perceptions[20], of prescribing antibiotics for several infectious diseases including RTIs among GPs (Butler *et al.* 1998, Tonkin-Crine *et al.* 2011b) and hospital doctors (Charani *et al.* 2013, Broom *et al.* 2014). However, there is a gap in GP qualitative research in terms of understanding their views and perceptions especially when treating elderly patients. Therefore, research must be undertaken to understand why and how GPs prescribe and consume antibiotics for UTIs (Duane *et al.* 2016). The literature review identified three studies on GPs' views and perceptions about antibiotics according to expanded search criteria that were reviewed and critiqued compared here and summarised in Table 16.

In Germany, Kuehlein *et al.* (2011) carried out a mixed methods study (observations, focus group discussions and interviews) to examine GPs' prescribing behaviour for LUTIs. The study was designed as a before–after study with a mixed three-step intervention between 1 January 2008 and 1 July 2009. The study recruited 18 GPs who were allocated to two focus groups, one comprising six GPs and the other comprising 12. Findings revealed that hospital teaching and training as well as letters from other specialists and hospital referral letters were the main drivers of GPs' current prescribing behaviour, which was thought to be more reflex-like than based on cognitive decisions. As this was a successful regimen in treating UTIs, GPs were not in favour of changing this practice. They could not see any difference in success between trimethoprim and fluoroquinolones. A combination of peer-group opinion and personal experience was said to be the main influence on treatment decisions. Moreover, some GPs admitted that recommendations were unknown to them, which had led to a noticeably sustained rise in trimethoprim prescribing. The study showed that GPs' practice was strongly influenced by evidence and peer-group opinion. Its limitations related to small sample size, GP selection bias, since all participating GPs were part of an ongoing project and knew each other, and the influence of the Hawthorne effect on GPs' prescribing. Additionally, the post-intervention change in prescribing behaviour was seen as a result of the study's influences on participating GPs, which could not be guaranteed in a larger population.

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[20] An individual's or group's unique way of viewing phenomena, involving the processing of stimuli and incorporate memories and experiences in the process of understanding. (McDonald 2012, p. 8).

In Sweden, Bjorkman *et al.* (2013) conducted qualitative GP interviews between October and November 2004 to explore GPs' views on resistance and UTI treatment. The study used two qualitative research methods: phenomenography to describe different ways of understanding AMR and content analysis to capture different views of UTI treatment decisions. The study recruited 20 GPs from 15 different primary care centres who were selected by purposive sampling to maximise variations in age, gender and geography. Interviews were semi-structured and contained open-ended questions relative to UTI signs and symptoms, UTI treatment, effects of treatment and resistance as well as probing questions. The phenomenographic analysis resulted in three different, mutually exclusive ways of viewing resistance in UTI treatment: 1) *'No problem, I have never seen resistance'*; 2) *'The problem is bigger somewhere else'*; and 3) *'The development of antibiotic resistance is serious and we must be careful'*.

The content analysis examined antibiotics choice and duration. During interviews, GPs discussed the recommendation of using alternative first-line antibiotics therapy with shorter duration. The common perception was that this applied only when treating a single patient to prevent recurrence because of resistance. Some GPs stated that each infection should be treated as a new one, so using a previously prescribed antibiotic agent is possible. The GPs also discussed using specific antibiotics for safety reasons, lack of records, patients' demands, the fear of side effects and costs. Adherence to alternative recommendations with careful prescribing of fluoroquinolones for UTIs was reported only among GPs who expressed view 3; GPs who expressed views 1 and 2 stated that they did not follow guidelines for all aspects of UTI in addition to sporadically using fluoroquinolones as a first-line therapy. Many GPs were reluctant to follow guidelines for shorter durations, too, owing to questionable efficacy or difficulty in changing previous ways of thinking. GPs with views 1 and 2 said that they followed guidelines but with longer durations or fluoroquinolones with shorter durations. Only those who expressed view 3 stated that they followed the guidelines for shorter courses of therapy. Although GPs with views 1 and 2 were aware of the recommendations and realised that their practice must change, a common belief was that being cautious would be enough. The findings suggested a relationship between adherence to UTI treatment guidelines and the perception that antibiotic resistance is a major problem. This study had inherent and significant limitations. First, interviews were performed in 2004, so awareness of resistance may have developed since then. Second, the study did not present the phenomenographical findings in the form of an outcome space figure, which is part of the analysis process. Additionally, it did not observe GPs' practice sufficiently to enable generalisation. Finally, content analysis is an analysis technique, not a qualitative method, and the analysis was thematic, not content based as the research team indicated (Vaismoradi *et al.* 2013).

In Ireland, Duane *et al.* (2016) conducted qualitative research to explore the prescribing culture and consumption of antibiotics for UTIs from GP and community standpoints. They carried out 15 interviews with GPs and six community focus groups with 42 participants using purposeful non-probability sampling. Core questions for GPs related to their practice for treating UTIs, antibiotics prescribing, antibiotics resistance and interventions to facilitate change in GPs' prescribing behaviour. Core questions for the community groups focused on health and GPs' consultations, antibiotics awareness, previous UTI experiences and interventions to facilitate community behaviour change in terms of consumption. Thematic analysis was used to identify emerging themes. Findings revealed that GPs were knowledgeable about resistance and the associated negative consequences, although they were more concerned about the long-term societal impact. They admitted that it was their responsibility to discuss resistance with patients, but saw diagnosis as simple, viewing antibiotics as necessary and preferring to prescribe them empirically for UTIs to reduce re-consultations. The study highlighted the importance and difficulty of capturing the complex interactions associated with antibiotics prescribing for UTIs. However, the small sample size and geographical constraints on recruitment were major drawbacks in this study.

In conclusion, three qualitative studies were identified that described GPs' views and perceptions about antibiotics prescribing to treat UTIs. All were conducted in European countries, namely, Germany (Kuehlein *et al.* 2011), Sweden (Bjorkman *et al.* 2013) and Ireland (Duane *et al.* 2016). All three studies included GPs as participants, although Duane *et al.* (2016) also had participants from the community with previous UTI experience. None of these studies discussed the elderly perspective. They varied in research design and data collection methods with focus groups (Kuehlein *et al.* 2011), phenomenographic and content analysis with semi-structured interviews (Bjorkman *et al.* 2013) and qualitative in-depth interviews as well as focus groups (Duane *et al.* 2016).

Qualitative evidence of GPs' views and perceptions about UTIs is limited in the UK, especially relating to elderly people. Collectively, three studies provide a wider image indicating that GPs' prescribing practice can be influenced by many factors and can vary greatly in terms of antibiotics choice, duration, frequency of prescribing, use of fluoroquinolones, adherence to guidelines and understanding the consequences of resistance (Bjorkman *et al.* 2013). The decision to prescribe antibiotics for UTIs comprises complex need recognition, information search and evaluation processes, governed by the relationship and interactions between the GP and the patient (Duane *et al.* 2016). GPs' antibiotics prescribing was mainly driven by former hospital training and common therapy whereas internal evidence and peer-group opinion were strong determinants for clinical decisions for UTIs (Kuehlein *et al.* 2011). Additionally, it was suggested that more research should be undertaken to understand the decision-making processes behind the continuing prescription of antibiotics for UTIs within the reality in which the behaviours exist, as this can lead to successful long-term behavioural change strategies (Duane *et al.* 2016).

Table 16: Summary of studies relevant to GPs' views and perceptions about antibiotics prescribing for elderly patients with UTIs

| Author | Country | Study Design | Data Source | N | Findings |
|---|---|---|---|---|---|
| Kuehlein *et al*. 2011 | Germany | Mixed methods | Focus groups | 18 GPs (6+12) | GPs' main driver for current GPs prescribing behaviour:<br>1) Hospital teaching and training.<br>2) Therapy seen in letters from other specialists.<br>3) Hospital referral letters.<br>Previous experience with a successful regimen in treating UTIs:<br>-GPs' agreed on lack of difference between the success of trimethoprim or fluoroquinolones.<br>-GPs' main influence on treatment decisions: peer-group opinion and personal experience.<br>-Some GPs admitted that they lack the knowledge about recommendations which resulted in sustained rise in trimethoprim prescribing. |
| Bjorkman *et al.* 2013 | Sweden | Phenomenography and content analysis | Semi-structured interviews | 20 GPs | Phenomenographic analysis:<br>Three different ways of viewing resistance in UTIs:<br>1) 'no problem, I have never seen resistance';<br>2) 'the problem is bigger somewhere else'; and<br>3) 'the development of antibiotic resistance is serious and we must be careful'.<br>Content analysis:<br>- Recommendations were only applicable for single patient to prevent UTIs recurrence.<br>- Some GPs stated that each infection should be treated as a new one and the use of previously prescribed antibiotic agent is something possible.<br>-The habit of using a specific drug due to its safety, lack of records, patients demand, fear of side effects and costs was also present in GPs statements.<br>-Adherence to UTIs alternative recommendations with careful prescribing of fluoroquinolones was only reported among GPs who considered resistance as serious threat.<br>-Many GPs were reluctant to follow-up guidelines for shorter durations owing to questionable efficacy.<br>-GPs who considered resistance as serious threat expressed view follow guideline including the use of shorter course of therapy.<br>-Some GPs were aware of the guidelines and realised their practice must be changed. |
| Duane *et al*. 2016 | Ireland | qualitative research | GPs in-depth interviews and community focus groups | 15 GPs + 42 community participants | -GPs were knowledgeable about resistance and the associated negative consequences<br>-Concern about resistance was more toward long term societal impact.<br>-GPs admitted that not many GPs' discuss resistance with patients and it was their responsibility to do that.<br>-UTI diagnosis was seen to be simple.<br>-Antibiotics were seen to be necessary for patients experiencing UTIs and preferred to prescribe them empirically to reduce reconsultations. |

### 2.7.4 Factors Influencing GPs' Antibiotics Prescribing

Several studies have explored factors responsible for GPs' prescribing antibiotics for infections such as sore throat (Kumar *et al.* 2003), RTIs (Brookes-Howell *et al.* 2012) and diarrhoea (Paredes *et al.* 1996) and for hospital doctors doing the same (Tan *et al.* 2006, Schouten *et al.* 2007). However, factors influencing GPs' prescribing for UTIs in relation to elderly patients have not been explored qualitatively. Moreover, no previous qualitative research has explored the differences in the factors influencing GPs' prescribing between adult and elderly patients. The literature review identified five studies on factors influencing GPs' antibiotics prescribing for UTIs that were critiqued and compared in the next paragraphs and summarised in Table 17.

In Iceland, Bjornsdottir and Hansen (2002) qualitatively explored physicians' reasons for prescribing antibiotics using in-depth semi-structured interviews with 10 GPs and field observation of three of them throughout 1995. They analysed the interviews and observational data using an open, axial and selective technique aimed at developing in-depth understanding rather than theories, to describe factors related to *'GPs' attitudes'*, *'uncertainty'*, *'time pressure'*, *'individual patients' characteristics' and 'perceived influence from colleagues with regards to antibiotics'*. Findings showed that GPs' attitudes towards prescribing were either restrictive owing to ecological considerations and spreading concern about resistance or liberal owing to concern about the possible consequences of withholding a necessary antibiotic. Most GPs mentioned uncertainty about whether to prescribe, owing to lack of solid diagnostic tests for some conditions, changes in treatment recommendations and complaints about side effects. Some GPs described time pressure as an occasional reason for prescribing when there was insufficient time to explain the inadequacy of antibiotics to patients. They also recognised that factors such as patients demanding antibiotics, having expectations, being able to comply with instructions and their general life situations play a role. Although GPs described colleagues' prescribing practice as an unimportant source of information, they were curious about it and felt it was crucial to discuss cases of doubt with colleagues regardless of any indicated uncertainty about their own superiority. Additionally, young GPs mentioned that peers can influence their prescribing habits to be more restrictive.

The study identified three different decision-making routes that can lead to antibiotic prescription. The first – *'that the infection can/will interfere with the patient's planned* *activities'* – relies on the belief that antibiotics might help and will not harm. The second – *'that the patient will not take no for an answer'* – is compounded by GPs' lack of resources to explain why antibiotics are not always appropriate. The third route suggests that *'GPs value patient autonomy more than patient welfare'*. Although several factors can influence antibiotics prescribing, helping patients to continue with daily activities was found to be the most important. One of this study's limitations was mixing the views of GPs on contracts and state-hired GPs. No attempt was undertaken to distinguish the views in either setting, which is unfortunate since the type of practice can influence the factors that emerge such as consultation fees and workload. Additionally, interviews were translated into Danish and selected quotations into English, which could have resulted in misinterpretations or mistranslations. Another limitation was the influence of the Hawthorne effect on the GPs who were observed in their workplace, which cannot be ruled out.

Again, in Iceland, Petursson (2005) conducted a qualitative phenomenological study to explore GPs' reasons for non-pharmacological antibiotics prescribing from 2000 to 2003. Data were collected through interviews with 16 GPs from different sites followed by iterative data analysis. The findings revealed five major factors for antibiotics prescribing: *'physician's personal character'*, *'physician's insecurity, uncertainty or anxiety'*, *'work pressure and fatigue'*, *'pressure from patients and their families'* and *'organisational factors'*. Factors related to the physician's character included earnings incentives, misinterpretation of patients' wishes, variable interpretation of symptoms, carelessness, unprofessionality, cheating to survive, variable attitudes, dislike of protocols, emphasis on subjective assessment and service mentality. Factors related to the physician's uncertainty included lack of continuous care, diagnostic uncertainty, distrust of colleagues, shrinking from conflict, transfer of patients' fears, lack of experience, fear of competition, fear of losing face, complaints and legal action, compromise as a back-up and reinforcing relationships with patients. Work pressure and fatigue associated factors included lack of time, means of survival by saving relationships between doctor and patients, antibiotics as a quick solution to end consultations, physicians in variable form, surrender to patients' inability to help themselves and surrender to extreme stimuli. Factors including misinformation and over-confidence in antibiotics, lower thresholds for tolerating discomfort, obsession with scheduled plans, craving for security, fear of illness, consciousness of consumer rights by pushy patients, job market difficulty and easy solutions without any discomfort were related to patients' or families' pressures on GPs to prescribe antibiotics. Some GPs perceived that the nature of healthcare's open access to physicians can partially justify the widespread use of antibiotics; additionally, lack of testing facilities and the effect of training processes were also mentioned as part of this problem. This study had some weaknesses, including the small sample size, which makes generalisation of the findings impossible, and that interviews were performed over a three-year period, during which time the researcher's and the GPs' views might have changed owing to new guidelines or policies.

Kotwani *et al.* (2010) conducted focus group discussions in India between May 2008 and September 2008 to identify antibiotics prescribing factors and appropriate interventions to promote rational use of antibiotics in a primary care setting. Thirty-six GPs (10 from public practice and 26 from the private sector) participated in three focus groups (one comprising 18 private sector GPs, one comprising eight public sector GPs and the third mixing two GPs from the public sector and eight from the private sector). Discussions focused on the motivations and behaviours that lead to antibiotics misuse. Data analysis was done through grounded theory, an inductive and iterative method. Findings were categorised into three broad themes: '*characteristic behaviour of doctor and patient*', '*laxity in regulation for prescribing and dispensing antibiotics*' and '*intervention strategies*'. Prescribing characteristics responsible for antibiotics misuse and overuse mainly related to doctors and patients. Doctor-related factors included inadequate knowledge, perceived patients' demands and expectations, diagnostic uncertainty, private practice sustainability and financial considerations, infection susceptibility, lack of time owing to public sector patient loads, antibiotics oversupply and near-expiry in the public sector and influences of medical representatives. Patient-related factors included compliance, improper dosage and self-medication by patients purchasing antibiotics over the counter and buying only as many tablets as they can afford or feel will provide them with a quick fix, lack of follow-up owing to expensive consultations in the private sector and long waiting hours in the public sector, patients seeking rapid cures by visiting several doctors when their condition does not improve within a day or two. Furthermore, doctors stated that if prescribing and dispensing of antibiotics by non-legalised persons, for instance, chemists or alternative medicine practitioners, ceased or was regulated then three-quarters of the problem would be solved, as their prescribing behaviour worsens the problem of antibiotics misuse. Interventions such as continuous medical education for doctors, education for patients' and families', advertisements on television and in newspapers, shared decision-making, guidelines for proper antibiotics use and stricter regulations for over-the-counter sales and prescribing by practitioners were suggested. This study had some weaknesses such as the small sample size of public sector GPs, from only five different municipalities within the West Delhi region, meaning that perceptions cannot be generalised. Additionally, the themes that emerged from the data analysis came mainly from the first focus group then were used in the subsequent two groups. Furthermore, some GPs within the mixed focus group might not have revealed their true behaviour, which could have influenced the study outcomes.

Vazquez-Lago *et al.* (2012) conducted a qualitative study in Spain from April 2009 to June 2009 to explore GPs' attitudes, knowledge and habits relating to antibiotics and resistance. They identified the attitudes and factors that influence antibiotics prescribing and compared their findings with other studies from countries with low antibiotics consumption and resistance rates. The study included 33 GPs working for the Spanish NHS in Galicia, an area with a high percentage of the population aged over 65. Data were collected through five focus groups, each comprising between four and 10 GPs. The focus group agenda was drawn up from a theoretical model published previously in a systematic review to capture GPs' factors and attitudes. Topics discussed related to the antibiotics prescribing process, misuse consequences and recommendations for improving antibiotics use.

The findings were grouped into predefined categories. The GPs considered UTIs to be one of the most common causes of antibiotics prescribing after RTIs. Moreover, antibiotics such as beta-lactams, particularly amoxicillin, macrolides, topical aminoglycosides and fluoroquinolones were said to be the most frequently prescribed. Antibiotics such as cephalosporins, tetracyclines, erythromycin and clarithromycin were less prescribed. Antibiotic selection was said to be guided by the patient's clinical profile, professional experience, clinical guidelines, pharmaceutical industry promotions and antibiotic price. Factors influencing GPs' antibiotics prescribing included fears related to the patient's characteristics, in particular being elderly, lack of confidence, fear of disease progression, complacency and patient dissatisfaction, that is, prescribing without real patient need or indication simply to satisfy patients, insufficient knowledge and external responsibility, relating to patients not taking antibiotics and pharmacies dispensing antibiotics without prescription, promotional pressures from pharmaceutical companies, the healthcare system, laboratories and other HCPs, and concern owing to lack of patient follow-up. Interestingly, GPs perceived antibiotics resistance as an important consequence of antibiotics misuse for UTIs but not lower RTIs. They also believed that resistance was a problem in hospitals rather than in the community, and attributed the causes of resistance to patients' non-compliance, antibiotics dispensing without prescription and inappropriate antibiotics prescribing by other HCPs, in particular dentists, community pharmacists and the veterinary industry. To improve antibiotics use, GPs stressed certain recommendations such as better population education, better access to diagnostic tests, improved communication between primary and secondary care, transfer of chronic patients to primary care, access to patients' electronic histories, continuous medical education, appointing professionals in hospitals for discussion and expert consultation, use of clinical guidelines without literal interpretation, use of delayed prescribing, development of a map of local resistance, and regular meetings with primary care pharmacies and local area management to discuss individual prescription profiles and highlight poor prescribing practice. The study did have some issues such as missing GP demographics data and qualifications, the small number and source of the participants, who were selected from a specific area of Spain and therefore reflected the attitudes of GPs in that particular area, and a lack of clear technique for data analysis.

In Portugal, Teixeira-Rodrigues *et al.* (2013) systematically reviewed the qualitative literature published between January 1987 and December 2011 to identify different factors, attitudes and knowledge that might influence physicians' perceptions about antibiotics prescribing. The review covered 35 studies, 18 of which included just physicians while the rest included hospitals, patients and parents. The physicians categorised the factors that had an impact on their antibiotics prescribing practice into two groups: intrinsic and extrinsic. The intrinsic factors described broadly socio-demographic factors such as previous clinical practice, years of practice, continuous medical education, university education and physicians' attitudes, including complacency, fear, ignorance, indifference, influence by other HCPs and confidence. The physicians considered diagnostic uncertainty and desire for a quick fix to be the basis of antibiotics misuse. The extrinsic factors were grouped into three categories. The first was patient-related factors, including signs, desire for a quick fix expressed by patients/carers, anxiety, symptoms of other clinical conditions, patient age, economic and social factors, and educational level. The second category – healthcare system-related factors – included ownership of practice location, time pressures, implemented policies/guidelines, influence of group exposure, communication and organisational models, accreditation level, inexistence of facilities to promote diagnostic tests, workflow, public health considerations, use of the same prescription several times and patient health insurance. The third category related to the influence of and financial incentives offered by pharmaceutical companies, and to cost savings to the patient or to the healthcare system.

The study concluded that attitudes were the most important factor affecting physicians' antibiotics prescribing. This review had some limitations, too. For one thing, it included only published studies, all of which were very heterogeneous, rendering it susceptible to bias. The heterogeneity was related to different settings (the studies were mainly from Europe and North America), workplaces (different realities present different factors), data collection methods and methods of analysis used. Additionally, there was an issue with the generalisability of the findings, since all of the reviewed studies used a small sample size. Moreover, as qualitative research is always criticised for its reliability, the trustworthiness of these studies must be considered within the inclusion criteria.

In summary, five studies described the factors influencing GPs' antibiotics prescribing practice in a primary care setting. All were conducted in European countries, namely, Iceland (Bjornsdottir and Hansen 2002, Petursson 2005), Spain (Vazquez-Lago *et al.* 2012) and Portugal (Teixeira Rodrigues *et al.* 2013) except for one study, which was conducted in India (Kotwani *et al.* 2010). All five included GPs as study participants, although one also looked at hospital doctors, parents and carers (Teixeira Rodrigues *et al.* 2013). Only one study briefly discussed the elderly as a population and UTIs without linking them (Vazquez-Lago *et al.* 2012). The studies varied in the forms of data collection, which ranged from focus group discussions (Kotwani *et al.* 2010, Vazquez-Lago *et al.* 2012), interviews (Bjornsdottir and Hansen 2002, Petursson 2005), field observation (Bjornsdottir and Hansen 2002) and literature review (Teixeira Rodrigues *et al.* 2013).

All five studies agreed that non-clinical factors, in addition to clinical factors, are important aspects of GPs' antibiotics prescribing decision-making. They explored several of these such as GPs' attitudes and personal characteristics, fears, diagnostic uncertainties, time pressures, patients' characteristics, perceived demand and patients' expectations. These factors were found to affect all prescribing stakeholders including patients, GPs, healthcare providers, the healthcare system and the general public, making antibiotics prescribing a complex issue to deal with (Teixeira Rodrigues *et al.* 2013). Four studies concluded that identifying factors that may influence GPs' antibiotics prescribing can be very useful in designing specific interventions and strategies to improve antibiotics use and help reduce resistance (Bjornsdottir and Hansen 2002, Kotwani *et al.* 2010, Vazquez-Lago *et al.* 2012, Teixeira Rodrigues *et al.* 2013).

Table 17: Summary of studies relevant to factors influencing GPs' antibiotics prescribing

| Author | Country | Study Design | Data Source | N | Findings |
|---|---|---|---|---|---|
| Bjornsdottir and Hansen 2002 | Iceland | Qualitative | Interview + field observation | 10 GPs + 3 GPs | -GPs' attitudes were either restrictive or liberal.<br>-Prescribing uncertainty owing to lack of solid diagnostic tests, changes in treatment recommendations and complaints about side effects.<br>-Time pressure can be an occasional reason for prescribing.<br>-Patients' factors include work and leisure activities, patients' behaviour in terms of expectations, pressure and being demanding, patients' compliance and patients' job situations.<br>-GPs felt curious about colleagues' prescribing habits.<br>-GPs felt it was crucial to discuss cases of doubt with colleagues.<br>-Young GPs prescribing habits can be influenced by peers to be more restrictive. |
| Petursson 2005 | Iceland | Phenomenological | Interview | 16 GPs | -Factors related to the physician's character: earnings incentive in the payment scale, misinterpretation of patients' presumed wishes, variable interpretation of symptoms, carelessness, unprofessional work, cheating to survive, variable attitudes, dislike of protocols, emphasis on subjective assessment and service mentality.<br>-Factors related to the physician's uncertainty: lack of continuous care, diagnostic uncertainty, distrust of colleagues, shrinking from conflict, transfer of patients' fear, lack of experience, fear of competition, losing face, complaints and legal action, compromise as a back-up and method of reinforcing relationships with patients.<br>-Factors related to work pressure and fatigue:<br>-Lack of time, saving relationships between doctor and patients, prescribing antibiotics to end consultations, physicians surrender to patients' inability to help themselves and surrender to extreme stimuli.<br>-Factors related to pressure from patients and their families:<br>-Misinformation and over-confidence in antibiotics, lower thresholds for tolerating any discomfort, obsession with scheduled plans, craving for security, fear of illness, consciousness of consumer rights by demanding and pushy patients, difficult job market and easy solutions without any discomfort.<br>-Factors related to organisation:<br>open access healthcare and lack of testing facilities and the effect of training processes. |
| Kotwani *et al.* 2010 | India | Qualitative | FGDs | 36 GPs | -Doctors related factors: inadequate knowledge, perceived patients' demands and expectations, diagnostic uncertainty, practice sustainability and financial considerations of doctors who work in private practice, consideration of infection susceptibility, lack of time owing to patient loads in the public sector, antibiotics oversupply and near-expiry in the public sector and influences of medical representatives. |

Continued Table 17

| Author | Country | Study Design | Data Source | N | Findings |
|---|---|---|---|---|---|
| Kotwani *et al.* 2010 | India | Qualitative | FGDs | 36 GPs | -Patient related behaviour: compliance, improper dosage and self-medication by patients, lack of follow-up, seeking rapid cures.<br>-Laxity in regulation: prescribing and dispensing of antibiotics by non-legalised persons.<br>-Dispensing antibiotics intervention strategies: CME, patients' and families' education, advertisements on television and in newspapers, shared decision-making, publishing and supplying guidelines, setting up stricter rules and regulations for OTC sales and prescribing by practitioners. |
| Vazquez-Lago *et al.* 2012 | Spain | Qualitative | FGDs | 33 GPs | -GPs considered UTIs to be one of the most common causes of antibiotics prescribing after RTIs.<br>-Antibiotics such as amoxicillin, macrolides, topical aminoglycosides and fluoroquinolones, were frequently prescribed.<br>-Antibiotics such as cephalosporins, tetracyclines, erythromycin and clarithromycin were less prescribed.<br>-Antibiotic selection was guided by the patient's clinical profile, professional experience, guidelines, pharmaceutical industry promotions and antibiotic price.<br>-Factors influencing antibiotics prescribing by GPs: fears related to the patient's characteristics, in particular being elderly; GPs' lack of confidence; fear of disease progression; complacency and the patient's dissatisfaction; GPs' insufficient knowledge and external responsibility, relating to patients not taking the antibiotics and pharmacies dispensing antibiotics without prescription; promotional pressures applied by pharmaceutical companies and the industry; the healthcare system; laboratories and other HCPs or prescribers; and concern owing to lack of patient follow-up.<br>-GPs perceived that antibiotic resistance was an important consequence of misuse of antibiotics in UTIs but not in lower RTIs.<br>-GPs believed that resistance was a problem in hospitals rather than at the community level<br>-Resistance was attributed to patients' non-compliance, antibiotic dispensing without prescription and inappropriate antibiotic prescribing by other HCPs, in particular dentists, community pharmacists and the veterinary industry.<br>-GPs stressed on population education, better access to diagnostic tests, improved communication between primary and secondary care, transfer of chronic patients to primary care, access to patients' electronic histories, CME, appointing professionals in hospitals for discussion and expert consultation, use of guidelines without literal interpretation, use of delayed prescribing, development of a map of local resistance, and regular meetings with primary care pharmacies and local area management to discuss individual prescription |

Continued Table 17

| Author | Country | Study Design | Data Source | N | Findings |
|---|---|---|---|---|---|
| Vazquez-Lago *et al.* 2012 | Spain | Qualitative | FGDs | 33 GPs | profiles and highlight poor prescribing practice to improve antibiotic use. |
| Teixeira Rodrigues *et al.* 2013 | Portugal | Systematic review of qualitative literature | Various | 18 GPs studies | Physicians categorised the factors into intrinsic and extrinsic.<br>-Intrinsic factors:<br>Socio-demographic: previous clinical practice, years of practice, continuous medical education, previous clinical practice and university education,<br>physicians' attitudes: complacency, fear, ignorance, indifference, prescribing attitudes of other HCPs and confidence.<br>-Others: diagnostic uncertainty and desire for a quick fix.<br>-Extrinsic factors:<br>Patient-related factors: signs, desire for a quick fix expressed by patients/carers, anxiety, symptoms of other clinical conditions, patient age, economic and social factors, and educational level.<br>-Healthcare system related factors: ownership of practice location, pressure of time, implemented policies/guidelines, influence of group exposures, communication and organisational model, implemented policies/guidelines, accreditation level, inexistence of facilities to promote diagnostic tests, workflow, public health considerations, use of the same prescription several times and patient health insurance.<br>-Other factors: pharmaceutical companies, cost savings to the patient or to the healthcare system and the financial incentives offered by pharmaceutical companies. |

CME continuous medical education, OTC over-the-counter FGDs focus group discussions

## 2.8 Research Rationale

Overall, the findings from the quantitative literature review on the epidemiology of UTIs suggest that UTIs increase significantly with advancing age, particularly in the over 85 age group (Ruben *et al.* 1995, Malmsten *et al.* 1997, Molander *et al.* 2000, Galatti *et al.* 2006, Czaja *et al.* 2007, Eriksson *et al.* 2010, Marques *et al.* 2012). Additionally, studies on antibiotics use revealed that elderly patients were prescribed antibiotics more frequently than other age groups (Wrigley *et al.* 2002) and that UTIs were one of the most common reasons for antibiotics prescription and consumption in the general population (Petersen and Hayward 2007a) and in the elderly population in particular (Friis *et al.* 1989, Leistevuo *et al.* 1997, Straand *et al.* 1998). However, various studies suggest the presence of a gap between recommended practice, namely guidelines, and actual GP practice, which can be irrational in many situations (Straand *et al.* 1998, Kahan *et al.* 2005, Taur and Smith 2007, McIsaac *et al.* 2008, Llor *et al.* 2011, Vellinga *et al.* 2011, Denes *et al.* 2012, Haasum *et al.* 2013). From another perspective, the review of the qualitative literature on GPs' antibiotics' prescribing revealed variations in GPs' perceptions and views about management and adherence to guidelines (Kuehlein *et al.* 2011, Bjorkman *et al.* 2013, Duane *et al.* 2016). These variations were found to be associated with numerous factors that could be related to GPs themselves, to patients, to the wider healthcare system or to society (Bjornsdottir and Hansen 2002, Petursson 2005, Kotwani *et al.* 2010, Vazquez-Lago *et al.* 2012, Teixeira Rodrigues *et al.* 2013).

Despite advances in the knowledge and understanding of various aspects of UTIs in elderly patients such as pathogenesis, diagnosis, resistance and antibiotic therapy (Ronald *et al.* 2001), there were number of gaps and issues revealed by the reviewed bibliographies and literature that deserve to be highlighted and explored. One of these issues was related to available evidence, which was often either outdated, based on data form settings other than GP surgeries or synthesised by none GPs (Hummers-Pradier and Kochen 2002). Additionally, newly published literature contains insufficient or repetitive information with few new thoughts or significant contributions to the field of knowledge. It was difficult in some studies to detect incidence, prevalence, antibiotics use and GPs' adherence to recommendations directly as the presented figures were not stratified according to patients' ages, which required manual recalculation of many of the figures. Furthermore, the literature review identified discrepancies between studies in terms of research designs and measurement units such as the use of percentages versus 100-person years in reporting UTI incidence or prevalence or the use of DDDs versus percentages in the case of drug utilisation studies. Moreover, assessing the appropriateness of antibiotics therapy in elderly patients with UTIs was based on adult guidelines, which usually lack special recommendations for this age group. This was in addition to recommendations differing greatly between countries in terms of antibiotics choices and estimated treatment durations. Finally, the generalisability of the findings was limited owing to small sample size in most of the studies. Differences in global populations meant that results were non-representative of other countries.

Surprisingly, the epidemiology of UTIs in the elderly and GPs' antibiotics prescribing practice relating to UTIs in the elderly appear to have received little or no attention in general (Hummers-Pradier and Kochen 2002) and in the UK in particular. The same applies to antibiotics drug utilisation (Willems *et al.* 2014), antibiotics prescribing against published national guidelines (Hummers-Pradier and Kochen 2002, High *et al.* 2005, Griebling 2014), variations in GPs' views and perceptions about the management of antibiotics for treating UTIs in elderly patients (Llor *et al.* 2011) and the factors that might influence or affect GPs' antibiotics prescribing for UTIs in elderly and adult patients (Vazquez-Lago *et al.* 2012, Bjorkman *et al.* 2013). It was suggested that more qualitative research needs to be conducted to understand the decision-making processes behind the continuing prescription and consumption of antibiotics for UTIs (Duane *et al.* 2016).

Although GPs' competencies were not in question, without this information, it might be assumed that elderly patients with UTIs are being well managed with appropriate evidence-based, cost-effective approaches and a high level of patient satisfaction. Bridging this knowledge gap might assist in developing strategies that can help to change GPs' prescribing behaviour, optimising and rationalising GPs' antibiotics prescribing and encouraging the rational use of available healthcare resources as well as enriching the literature on UTI research. To achieve this, quantitative research on drug utilisation is needed – one of the actions included in the UK's five-year antimicrobial resistance strategy (Davies and Gibben 2013) – in addition to qualitative phenomenographic research into the variations in GPs' views as well as the factors influencing their prescribing.

## 2.9 Research Aim and Questions

The previous sections gave an overview of how common UTIs are in elderly patients. The work described in this thesis was aimed at providing insight on GPs' antibiotics prescribing for UTIs in elderly patients in the UK. A mixed method approach was adopted to meet the thesis research questions, which are:

1. What is the prevalence of UTIs in elderly patients who visit GP surgeries in the UK?
2. What are the patterns and trends of GPs' antibiotics prescribing for UTIs in elderly patients?
3. Is GPs' antibiotics prescribing practice for UTIs in elderly patients in line with the SAPG decision aid for diagnosis and management of suspected urinary tract infection (UTI) in older people?
4. Are there variations in GPs' views and perceptions about antibiotics for UTIs in elderly patients?
5. What are the factors that might influence or affect GPs' antibiotics prescribing for UTIs in the elderly compared with adult patients?
6. What are the impacts of the findings of this thesis on future research?

## 2.10 Summary

This chapter has reviewed the relevant literature on GPs' antibiotics prescribing for UTIs from quantitative and qualitative perspectives, explained the rationale for this research and listed the study aims and research questions to be answered. The findings from the literature review have shown that further work is needed to fill the gaps in the current knowledge of UTIs in elderly patients in terms of recognising GPs' antibiotics patterns and trends of prescribing, exploring GPs' views about antibiotics for UTIs in elderly patients and identifying the factors influencing GPs' antibiotics prescribing for UTIs. The next chapter describes the research framework and methods used in this thesis to fill these gaps.

# Chapter 3 Research Methodological Approaches and Methods

## 3.1 Introduction

This chapter outlines the methodological approaches and methods undertaken in this research. In the next section, each was briefly outlined and the rationale behind its selection explained. Then the methods implemented were described, along with the analysis process followed to obtain the results and findings for each part of the research. The reason for following this structure was to provide the reader with overview on some important aspects of the method used before describing the research methodology. Owing to the different nature of employed approaches, structure and content may vary from one approach to another.

## 3.2 Research Methodological Approaches

A research methodological approach can be described as a framework that brings together broad research assumptions into a detailed plan, data collection method(s), analysis of data and interpretation of research findings (Harwell 2011, Creswell 2014). Different research questions and hypotheses demand adoption of different research approaches (Marczyk *et al.* 2005). Research methodological approaches can be mixed methods, quantitative or qualitative (Harwell 2011, Creswell 2014).

The mixed methods approach has become more popular over the last two decades (Harwell 2011, Creswell 2014, Ozawa and Pongpirul 2014) especially in healthcare and prescribing research (Lapane *et al.* 2011, Solomon *et al.* 2012, Reynolds *et al.* 2016). Mixed methods research can be defined as:

> *'The class of research where the researcher mixes or combines quantitative and qualitative research techniques, methods, approaches, concepts or language into a single study. Mixed methods research also is an attempt to legitimate the use of multiple approaches in answering research questions, rather than restricting or constraining researchers' choices (i.e., it rejects dogmatism). It is an expansive and creative form of research, not a limiting form of research. It is inclusive, pluralistic, and complementary, and it suggests that researchers take an eclectic approach to method selection and the thinking about and conduct of research'* (Johnson and Onwuegbuzie 2004, pp. 17-18).

Owing to the differences between qualitative paradigms, which are interpretive and constructionist, and quantitative paradigms, which is positivist, it has often been argued that the two approaches are incompatible and cannot be mixed (Mays and Pope 2000, Pope and Mays 2006, Harwell 2011). However, running a qualitative study alongside a quantitative approach can be useful as both share commonality in their goal of understanding the world in which individuals live, allowing researchers to view problems from different perspectives, contextualising information and linking it to understanding and improving the human condition (Creswell 2014). The rigour of this research process can be especially useful in disciplines where the complexity of phenomena requires data from a large number of perspectives, as in healthcare research (Sale *et al.* 2002, Denzin and Lincoln 2011, Harwell 2011). Additionally, the mixed methods approach has the ability to quantify hard-to-measure constructs, provide illustrations of context for trends, examine processes and experiences along with outcomes to capture a wider picture for phenomenon studies, apply *'triangulation'*, which involves comparing data from the two approaches in an attempt to validate findings and demonstrate greater credibility when there is agreement between findings (Johnson and Onwuegbuzie 2004, Denzin and Lincoln 2011, Harwell 2011).

Using a mixed methods approach can provide the opportunity to outweigh the inherent weaknesses of both methods, capitalise on inherent method strengths, counteract unavoidable method biases and provide insights not possible when only a qualitative or a quantitative approach is used (Harwell 2011, Creswell 2014). For instance, quantitative methods can provide a robust result about the magnitude of a specific problem. In the case of antibiotics prescribing, measures determine GPs' adherence to good practice points. However, a quantitative method cannot contribute to understanding and capturing more complex issues that may have influenced GPs' behaviour in association with adherence to good practice points. Including a qualitative research element to capture this phenomenon can enable exploration of a range of issues, such as non-obvious factors that may come to light through this more in-depth methodology (Pope and Mays 1995). Qualitative research can provide an understanding of perceptions, views and concepts, and explore issues that may have influenced GPs' adherence to good practice points within a naturalistic setting, in this case primary care. Therefore, using a research approach that incorporates both qualitative and quantitative methods can yield differing types of data and perspective (Harwell 2011, Creswell 2014).

Despite numerous benefits of a mixed methods approach, however, evaluating the findings can be complicated by the differing epistemological[21] assumptions across the methods. Patton explained:

> *'In real-world practice, methods can be separated from the epistemology out of which they have emerged'* (Patton 2002, p. 136),

to which Flick added that:

> *'Mixed methodology approaches are interested in pragmatic links of qualitative and quantitative research in order to end the paradigm wars of earlier times'* (Flick 2007, p. 9).

Adopting a pragmatic theoretical perspective is therefore a reasonable solution to overcoming these differences as highlighted and recommended by different researchers (Johnson and Onwuegbuzie 2004, Teddlie and Tashakkori 2009). Adopting a pragmatist paradigm allows researchers to adopt whichever method is most suitable for a particular question or area of research without being restricted to one methodology and viewpoint (Sale *et al.* 2002) and to be flexible, often through using both qualitative and quantitative research methods (Teddlie and Tashakkori 2009). Therefore, in studying GPs' antibiotics prescribing for elderly patients with UTIs, a pragmatic approach supports the use of both qualitative and quantitative approaches.

### 3.2.1 Use of Mixed Methods Approach

Owing to the nature of the research aim and research questions, a comprehensive mixed methods approach was adopted with an explanatory sequential approach (Ozawa and Pongpirul 2014), that is, a quantitative study to set-up the scene followed by a qualitative study. First, a quantitative drug utilisation study was carried out to explore the prevalence of UTIs as in (Czaja *et al.* 2007, Eriksson *et al.* 2010, Caljouw *et al.* 2011), antibiotics prescribing patterns and GPs' adherence to good practice as in (Llor *et al.* 2011, Denes *et al.* 2012, Haasum *et al.* 2013). Second, a qualitative study using a phenomenographic method with two analytical techniques was performed to gain an in-depth understanding of GPs' views and perceptions as it was employed by (Kuehlein *et al.* 2011, Bjorkman *et al.* 2013, Duane *et al.* 2016) in addition to the factors influencing their prescribing practice

[21] Refer the manner by which knowledge is constructed and the relationship of the knower to the known' (Guba and Lincoln 1994, p. 108).

for treatment of UTIs in adults and the elderly (Bjornsdottir and Hansen 2002, Petursson 2005, Kotwani *et al.* 2010, Vazquez-Lago *et al.* 2012, Teixeira Rodrigues *et al.* 2013).

#### 3.2.1.1 Quantitative Research Approach

##### *3.2.1.1.1 Drug Utilisation Review Background*

###### *3.2.1.1.1.1 Definitions and Historical Overview*

Drug utilisation research (DUR) has gained in popularity as an essential and special type of pharmacoepidemiology[22] studies. DUR has the ability to describe the nature, extent and causes of drug exposure (Birkett *et al.* 2003). It is multidisciplinary research that is recognised as a valuable and legitimate quality assurance tool for any drug therapy (Cooke 1991, Blackburn 1993). Interest in DUR began in the 1960s and is still increasing (Hasle 2002).

The beginnings of drug utilisation research were sparked by initiatives taken in the UK and Northern Europe in the mid-1960s. The creative leading work of Arthur Engel in Sweden and Pieter Siderius in the Netherlands in 1968 enlightened the field as to the importance of comparing drug use and consumption among different regions and countries (Birkett *et al.* 2003). The terms *'drug utilisation review'*, *'drug usage review'*, *'drug use review'* and *'drug use evaluation'* are more or less synonymous and can be used interchangeably (Cooke 1991).

WHO defined DUR in 1977 as:

> *'Studies or research related to marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences'* (Birkett *et al.* 2003, p. 8).

This definition covers most, if not all, aspects of drug epidemiology, including methodological approaches as well as analytical and descriptive evaluations. However, some researchers recommended the incorporation of drugs development in relation to health priorities into this definition (Lunde and Baksaas 1987). In North America, a more

[22] The study of the use and effects/side-effects of drugs in large numbers of people with the purpose of supporting the rational and cost-effective use of drugs in the population thereby improving health outcomes (Birkett et al. 2003, p. 8).

structured and narrower definition was used in the 1970s to define drug utilisation studies, namely:

> *'Research or studies related to the prescribing, dispensing and ingesting of drugs'* (Brodie 1971, p. 1).

In both definitions, all non-pharmacological factors (behavioural, socio-anthropological and economic) that influence drug utilisation were recognised and considered either explicitly or implicitly (Lee and Bergman 2012).

In Europe, countries such as Scandinavia, Northern Ireland and Scotland have been recognised as pioneers in this field of research, both nationally and internationally (Sacristan and Soto 1994, Gama 2008, Sachdeva and Patel 2010). Furthermore, DUR studies in these countries have been designed to describe and compare variations in patterns of use of specific groups of drugs according to geographical regions and seasons of the year (Gama 2008); whereas studies from the USA were primarily designed as part of institutional-level interventions or as part of local health programmes (Blackburn 1993). Historically, the first group in the UK (UK DURG) was founded in 1989 by a multidisciplinary group of researchers who noticed a lack of awareness of drug utilisation research among pharmacologists (McGavock 1998).

#### *3.2.1.1.1.2 Classification and Uses of Drug Utilisation Studies*

Drug utilisation studies can be broadly categorised as either qualitative or quantitative (LeLorier *et al.* 2003). Qualitative studies are often designed to assess the appropriateness of drug utilisation, usually by linking prescription data to the reasons for prescribing the drug (Birkett *et al.* 2003, Lee and Bergman 2012). Quantitative studies are descriptive studies of drug use frequency designed with the aims of (Birkett *et al.* 2003, Lee and Bergman 2012):

- measuring quantities and comparing variations in drugs prescribed or consumed over a specific period of time and in a specific geographical region (national, regional, local) and/or season;
- estimating disease prevalence according to drug consumption rates prescribed to manage the disease under investigation;
- investigating patterns of drug utilisation over a specific period of time and identifying regions of possible under- or over-utilisation of drugs; and

- estimating drug consumption and use according to specific variables such as age, sex and social class.

DUR studies can be further classified according to the timing of data collection, that is, methodology, into three types. Each type has its own features that serve a specific study purpose (Anis *et al.* 1996). These studies are as follows (Wertheimer 1988, Birkett *et al.* 2003):

1. prospective studies – in this type of study, the prescribed drug will be compared to predetermined criteria before the patient receives the drug. This type of study is recognised for its preventive potential, and for being individual patient-centred in its interventions;
2. concurrent studies – in this type of study, the prescribed drug will be reviewed during the course of therapy. This type of study is ideal when drug adjustments may be necessary based on ongoing diagnostic and/or laboratory tests; and
3. retrospective studies – in this type of study, historical patients or drugs data are used. These studies involve reviewing drug prescribing and use after the drugs have been dispensed; therefore, they are of some value. Although this is the easiest and least costly approach, there is no opportunity to modify the therapy for the patients on whom the data were collected.

#### *3.2.1.1.1.3 Drug Utilisation Conceptual Framework*

Lipton and Bird (1993) elucidated a conceptual DUR framework model based on assumptions related to factors that may either hinder or improve the quality of drug prescribing within the context of other important factors (Lipton and Bird 1993). These factors include prescriber factors, system factors and patient and family factors as presented schematically in Figure 13. The model describes how DUR interventions relate to drug prescribing and dispensing. In the case of prospective DUR, the influence can be seen on the current process of prescribing and dispensing through considering prescriber's and patient's factors, that is, the micro-level; whereas retrospective DUR can influence future prescribing and dispensing, which can be a target for healthcare authorities and agencies when improving drug prescribing policies, that is, the macro-level (Lipton and Bird 1993). It can result in the development of interventions that can counteract many of the detrimental influences of patients, prescribers and system factors and reinforce positive outcomes on the quality of drug prescribing, improving patients' clinical outcomes and utilising healthcare institutions' financial resources more prudently. It is important to realise that DUR is targeted towards identifying and correcting avoidable or preventable prescribing problems such as drug dosage and duration. However, DUR cannot identify or correct unavoidable ADRs that result from appropriate use of drug therapies (Lipton and Bird 1993).

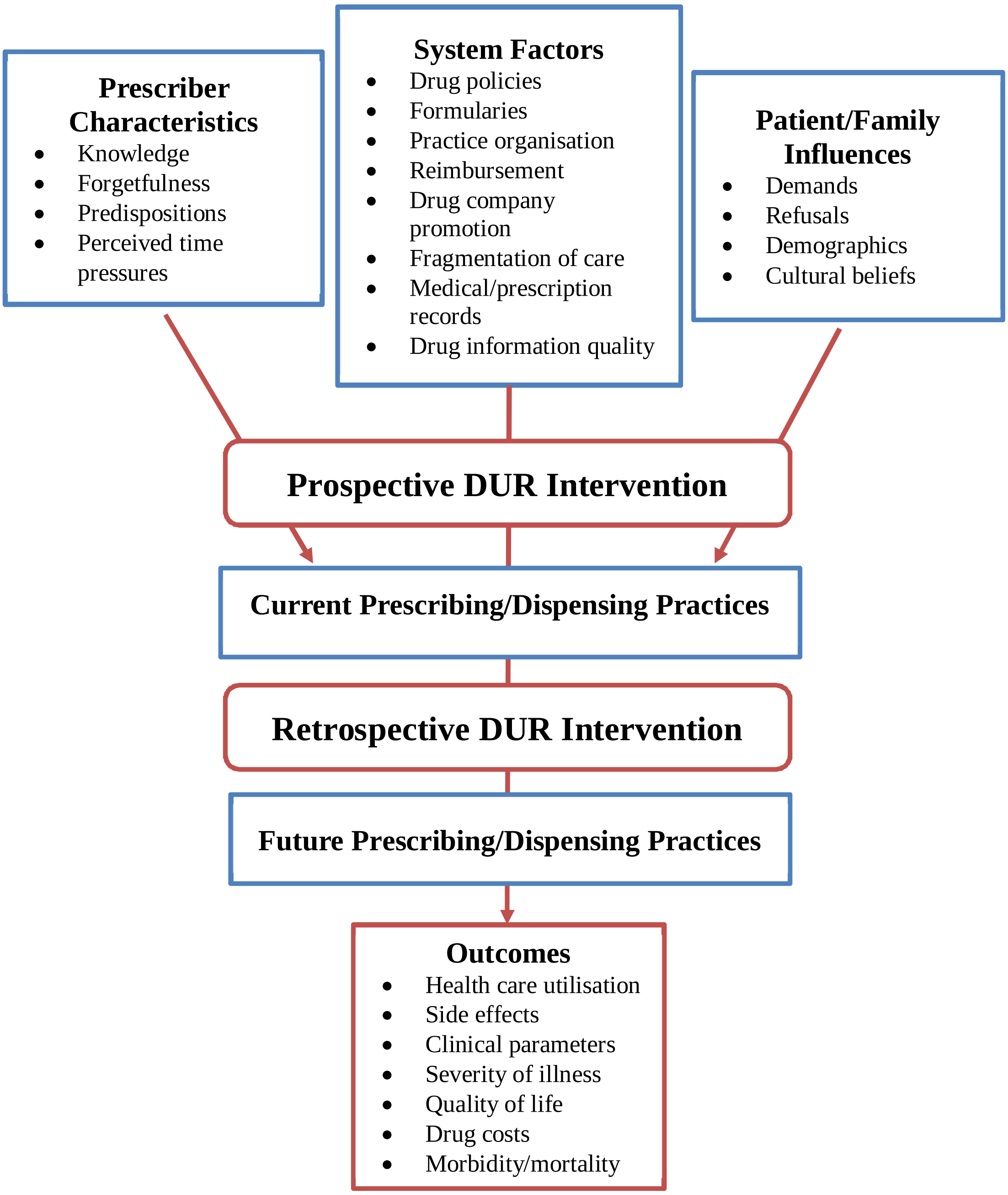



Figure 13: Factors conceptualised in DUR (Lipton and Bird 1993, p. 1072)

#### *3.2.1.1.1.4 Drug Classification Systems Used in Drug Utilisation*

Since the introduction of DUR, researchers have felt it necessary to have a common drug classification system to describe drug assortment in a region or country so that drug utilisation comparisons can be made among drugs at national and international levels (Truter 2010). Having such a classification system would make it easy for researchers uniformly to collect and aggregate drug utilisation data to audit different patterns of drug use, detect drug use issues and problems, and initiate interventions and monitor their outcomes. In general, drugs can be classified in various ways according to their indications, therapeutic or pharmacological classes, mode of action, or according to chemical structure (Birkett *et al.* 2003, Lee and Bergman 2012).

Currently there are two widely used classification systems based on identical ideologies (Birkett *et al.* 2003, Lee *et al.* 2013). The first is Anatomical Therapeutic (AT) classification, developed by the European Pharmaceutical Market Research Association (E*ph*MRA). In this system, drugs are classified into groups on three or four different levels. The E*ph*MRA classification system is used worldwide by IMS Health to provide market research statistics to the pharmaceutical industry. The second system is Anatomical Therapeutic Chemical (ATC) classification, developed originally by the Norwegian Medicinal Depot, which became a WHO Collaborating Centre for Drug Statistics Methodology. This classification system was modified and extended from the E*ph*MRA system by introducing a therapeutic/pharmacological/chemical subgroup as the fourth level and chemical substance as the fifth level. The WHO classification system was recommended to be used as a tool to generate statistical reports when international drug utilisation comparisons are required.

To demonstrate how both classification systems work, trimethoprim has been used to explain the structures of the code in Table 18. Owing to the various technical differences between the two classification systems, data obtained by the two classification systems are not directly comparable (Birkett *et al.* 2003, Shalini *et al.* 2010).

Table 18: Trimethoprim code structures showing the difference between AT and ATC classification systems

| Level | Description | Code | WHO | Code | EphMRA |
|---|---|---|---|---|---|
| 1st | Main anatomical group | J | Antiinfectives for systemic use | J | General antiinfective systemic |
| 2nd | Main therapeutic group | 01 | Antibacterial for systemic use | 1 | Systemic antibacterial |
| 3rd | Therapeutic/pharmacolog-ical subgroup | E | Sulphonamides and trimethoprim | E | Trimethoprim and similar formulations |
| 4th | Chemical/therapeutic /pharmacological subgroup | A | Trimethoprim and derivatives | - | Not applicable |
| 5th | Subgroup for chemical substance | B | Short-acting sulphonamides | - | Not applicable |

### *3.2.1.1.1.5 Drug Utilisation Databases*

The sources of drug utilisation databases vary widely from one country to another according to several factors such as the level of complexity of record-keeping and saving, methods of data collection, methods of data analysis, healthcare system-related reporting and operational considerations (Gama 2008). Databases used for drug utilisation studies can be either diagnosis linked or non-diagnosis linked. The former type provides information about drugs consumption for particular diseases and outcomes while the latter type provides information only about drugs consumption in a specific population. The majority of these databases lack information on patients' morbidity, so are generally used to generate drug utilisation statistical reports and descriptive studies of drug consumption patterns (Birkett *et al.* 2003).

Currently, available databases can be categorised as administrative, medical, pharmaceutical or commercial in origin (Truter 2010). In Europe, the automated databases are primarily medical records databases in origin and they were developed to assist researchers in performing epidemiological studies. The USA has databases that are mostly administrative in origin, which were developed for handling claims and payments for clinical services and therapies (Lee *et al.* 2013).

Electronic medical records (EMRs) databases were introduced to medical practice nearly three decades ago (Takahashi *et al.* 2012). They are population based, that is, longitudinal, in their nature and they were developed as a result of moving towards more computerised medical services to capture patients' related data. EMRs databases normally contain patients' related administrative and clinical data, they are maintained primarily for documenting patients' conditions, treatments and outcomes, and they can be anonymised for the purpose of research (Ogdie *et al.* 2012). EMRs databases have many unique advantages, most important among which is that the validity of the diagnosis data is far better than in other forms of database, as these data are being used mainly for medical care purposes. However, there are also unique disadvantages, especially the uncertain completeness of the data from some GPs and practice sites (Ogdie *et al.* 2012).

EMRs databases can offer unique opportunities to HCPs, researchers and decision-makers when they are extracted and analysed properly. They can be very useful resources for planning and monitoring different healthcare services and measuring the quality of services and care provided. The strengths of data collected from UK GP practices are that they are population based, population representative and contain information on patients' conditions, treatment, outcomes and use of healthcare services (Gnani and Majeed 2006). In the UK, several EMRs databases are available in GP surgeries. However, because much of these fall beyond the scope of this thesis, only three longitudinal databases will be discussed in the next section, more specifically the Clinical Practice Research Datalink (CPRD), The Health Improvement Network (THIN) and the Intercontinental Marketing Services-Disease Analyzer (IMS-DA). Table 19 compares these three UK-based databases. Lists details of data supplied by these databases can be found in Appendix 4.

The CPRD is the world's largest computerised, longitudinal EMRs database for primary care (Herrett *et al.* 2015). Established in 1987 in London, it was known at that time as Value Added Medical Products (VAMP). With time, the data continued to grow and it became the GPRD in 1993. In 2012, the GPRD expanded dramatically to become the CPRD. The database contains regularly collected anonymised electronic health record data from GP practices in England, Wales, Scotland and Northern Ireland. The database contains the health records from over 674 practices around the UK, which equates to over 13 million patients representing more than 6.9% of the UK's total population and 5 million active patient records (NIH 2014, Herrett *et al.* 2015). Access to the latest version can be purchased at (www.cprd.com) via academic collaboration or by paying a fee.

The second database, THIN, represents a joint collaboration between two companies: In Practice Systems (INPS), which developed the Vision software used by GPs in the UK to manage patients' data, and IMS Health, which provides access to data for use in medical research. Since it was established in 2002, THIN contains the health records from 587 GP surgeries around the UK, which equates to more than 12 million patients records and over 3.6 million active patients that represent 5.67% of the UK's population (up to July 2013)

(UCL 2013). Extracted data from THIN is organised into seven categories. Recently, THIN became part of IMS Health. Access to the latest version can be obtained at (www.csdmruk.imshealth.com) via academic collaboration or by paying a fee.

The third database, IMS-DA, previously known as MediPlus, is maintained by IMS Health, which is an international healthcare information service and technology company. IMS Health specialises in collecting and interpreting anonymised health information within the UK and across the world. Most often, IMS Health is considered the only source of information on aspects related to drug utilisation globally. The complex and secure IMS database represents an invaluable source for pharmacoepidemiological studies. IMS-DA is one of the largest longitudinal clinical databases in the world, derived from the electronic clinical records maintained by GPs in the course of providing care for their patients, and anonymised for research purposes (Dietlein and Schroder-Bernhardi 2002). The database contains the health records from over 130 practices around the UK, which equates to over 2 million patients that represent almost 3.1% of the UK's population, and over 95 million prescriptions prescribed by more than 500 GPs (Pillay *et al.* 2010, Hsia *et al.* 2012). The database has been validated in several published studies and found to be reliable and accurate with a good correlation between the database population and the UK population in terms of age distribution and male-to-female ratio (Pillay *et al.* 2010). Access to the latest version can be purchased at (www.imshealth.com) via academic collaboration or by paying a fee.

Table 19: Summary comparison between the most commonly used databases in the UK (Murray *et al.* 2013a, UCL 2013, NIH 2014, Herrett *et al.* 2015)

| Database | Diagnoses/clinical code | System | Strengths | Limitations |
|---|---|---|---|---|
| **CPRD** | **Read code** | **VAMP System** | -Data are broadly representative of national population (covers about 6.9% of UK population)<br>-The quality and completeness of recording are high and validity have been reported to be high<br>-Easy to perform denominator counts to allow calculation of prevalence and incidence rates<br>-Reliable<br>-Complete<br>-Additional services are provided by the CPRD group such as questionnaires to GPs to obtain further information<br>-Data linked to HSE<br>-Data have been widely used by researchers and over 1000 articles published in peer-review journals | -Data are primarily collected for clinical management not for research purposes<br>-It requires intensive training to use data and knowledge of relational databases<br>-There is no information on hospital data, length of stay and prescriptions<br>-There may be misclassification or coding errors<br>-OTC prescriptions are not recorded<br>-Prescription records are not directly linked with diagnoses.<br>-Medication adherence is not recorded<br>-Only issued prescriptions are recorded<br>-Information on individual socioeconomic status and ethnicity are not recorded<br>-Expensive |
| **THIN** | **Read code** | **INPS** | -Data are broadly representative of national population (covers 5.67% of UK population)<br>-The database contains useful 'Acceptable Mortality Reporting' filter to avoid the danger of "immortal period" bias<br>-Reliable<br>-Complete<br>-Anonymised comments and Townsend deprivation scores are available<br>-Additional service are offered such as questionnaires to GPs to obtain further information<br>-Data linked to HSE<br>-Data have been widely used by researchers and over 540 articles published in peer-review journals | -Data are primarily collected for clinical management not for research purpose<br>-There is no information on hospital tests, length of stay and prescriptions<br>-There may be misclassification or coding errors<br>-OTC prescriptions are not recorded<br>-Ethnicity is not recorded<br>-No direct link between prescriptions and diagnoses<br>-Only issued prescriptions are recorded<br>-The database was newly available so little validation work had been conducted at the time<br>-Medication adherence is not recorded<br>-Expensive |

Continued Table 19

| Database | Diagnoses/clinical code | System | Strengths | Limitations |
|---|---|---|---|---|
| **UK IMS-DA** | **ICD-10, Read code** | **Meditel System** | -Data are broadly representative of national population (covers about 3.1% of UK population)<br>-Allow researchers to use population based study designs for general practice setting<br>-Large population<br>-Minimizing selection bias<br>-Improving validity<br>-Improving generalisability<br>-Reliable<br>-Complete<br>-Direct link between diagnosis and prescription<br>-Test results linked to diagnoses<br>-Very good age and gender correlation between database population and UK population<br>-GPs are broadly representative of those in the UK population<br>-Easy to obtain denominator counts to allow calculation of prevalence and incidence rates<br>-Free from observer and recall bias<br>-No specific computerised tool needed to use data<br>-License is inexpensive<br>-Data have been widely used by researchers and over 200 articles published in peer-review journals | -Data are primarily collected for clinical management not for research purpose<br>-Only issued prescriptions are recorded<br>-Under-representation of smaller practices<br>-Over-representation of practices in Scotland and Northern Ireland<br>-There may be misclassification or coding errors<br>-Data on lifestyle factors such as smoking status, and body mass index may be incomplete<br>-Only records prescriptions that are issued, therefore primary compliance and actual drug use are unrecorded<br>-No additional services offered such as questionnaires to GPs<br>-Knowledge of relational databases and general practice essential<br>-Limited number of studies available on validity of the IMS-DA database<br>-Lack of patient socioeconomic status<br>-Completeness of data<br>-Occupation and employment status are rarely recorded<br>-Not all medications are linked to a diagnosis<br>-Medication adherence is not recorded<br>-Loss to follow-up over time if patient transfer out of the practice or if the practice ceases to participate in the database |

OTC: over-the-counter; HSE: Hospital Episode Statistics; INPS: In practice systems; VAMP: Value Added Medical Products

### 3.2.1.2 Qualitative Research Approach

Qualitative research methods have become very popular in the field of healthcare (Britten 2005). As research techniques, they have the ability to answer questions through themes and ideas generation that are equally valid but quite different from quantitative research methods (Holloway 2005). Qualitative research has many features and strengths, one of which is its ability to study people in their natural world or setting rather than in a non-natural world or setting. Furthermore, it enables researchers to interact with people in their own language and terminology (Tracy 2013). Another feature is that it tries to interpret and explain social phenomena, behaviours and interactions in terms of the meanings people bring to them. In healthcare, qualitative research is very beneficial in interpreting complex human behaviours such as health decision-making (Shen *et al.* 2015) and patients' adherence to drugs (Holt *et al.* 2014). Additionally, it enables researchers to mix several different qualitative methods such as observing people closely in their own field, that is, observation, reading what they have written, that is, surveys, and interacting with people, that is, focus groups and interviews (Silverman and Marvasti 2008). The term '*qualitative research*' is a broad term used to describe a wide range of diverse research approaches with regard to research aims, theoretical assumptions, understanding of phenomena under investigation, methodological focus and methods applied (Flick *et al.* 2004). Examples of these approaches include grounded theory, ethnography, phenomenography, phenomenology, content analysis and field studies (Flick *et al.* 2004). The selection of a research approach should be directed by the research question or aim and the theoretical assumptions adopted (Lundborg *et al.* 1999). The rationale for choosing a qualitative research approach over a quantitative research approach was that qualitative research mainly concerns the development of concepts that assist researchers in better understanding phenomena in their natural settings by emphasising the meanings, views and experiences of the participants (Pope and Mays 2009).

#### *3.2.1.2.1 Phenomenography Background*

##### *3.2.1.2.1.1 Definitions and Historical Overview*

The word '*phenomenography*' was derived from two Greek words: '*phainomenon*', which refers to appearance, and '*graphein*', which refers to description (Hasselgren and

Beach 1997). This approach has been used widely in the field of educational research, having evolved originally from the work performed by Marton and colleagues at the University of Gothenberg, Sweden, in the 1970s. However, the term phenomenography did not appear in the English literature until the early 1980s (Marton 1986). Phenomenography has also been used in several healthcare services research projects (Barnard *et al.* 1999, Sjöström and Dahlgren 2002, Larsson and Holmström 2007).

Phenomenography is an interpretive, descriptive, second-order approach that has the ability to describe variations in human understanding, meaning, ideas and thoughts relating to a particular phenomenon within a group of individuals (Marton 1981). It is most frequently described as:

> *'A research method for mapping the qualitatively different ways in which people experience, conceptualise, perceive, and understand various aspects of, and various phenomena in, the world around them'* (Marton 1986, p. 31).

A more recent description of phenomenography by Marton and Booth focused on:

> *'Variation in ways of experiencing things'* (Marton and Booth 1997, p. 110).

#### *3.2.1.2.1.2 Ontological and Epistemological Stances in Phenomenography*

Phenomenography evolved from a strongly empirical origin rather than a theoretical or philosophical frameworks. Since phenomenography has a characteristic ontological[23] position, it differs from other qualitative research approaches. Phenomenography adopts a non-dualistic ontology, known as constitutionalism. Ontologically, phenomenography relates to the nature of existence, based on the assumption that an individual and the world are interrelated through the individual's lived experience of the world (Marton and Booth 1997, Sandberg 2000). Figure 14 illustrates phenomenography's focus in relation to subject, object, researcher and the world.

Phenomenography perceives experience as a relationship between the object, that is, the world, and the subject, that is, the individual, as this citation by Marton (2000) demonstrates:

> *'From a non-dualistic ontological perspective, there are not two worlds: a real, objective world, on the one hand, and a subjective world of mental*

[23] Refer to nature of reality (Guba and Lincoln 1994, p. 108).

*representations, on the other. There is only one world, a really existing world, which is experienced and understood in different ways by human beings. It is simultaneously objective and subjective* (Marton 2000, p. 105).

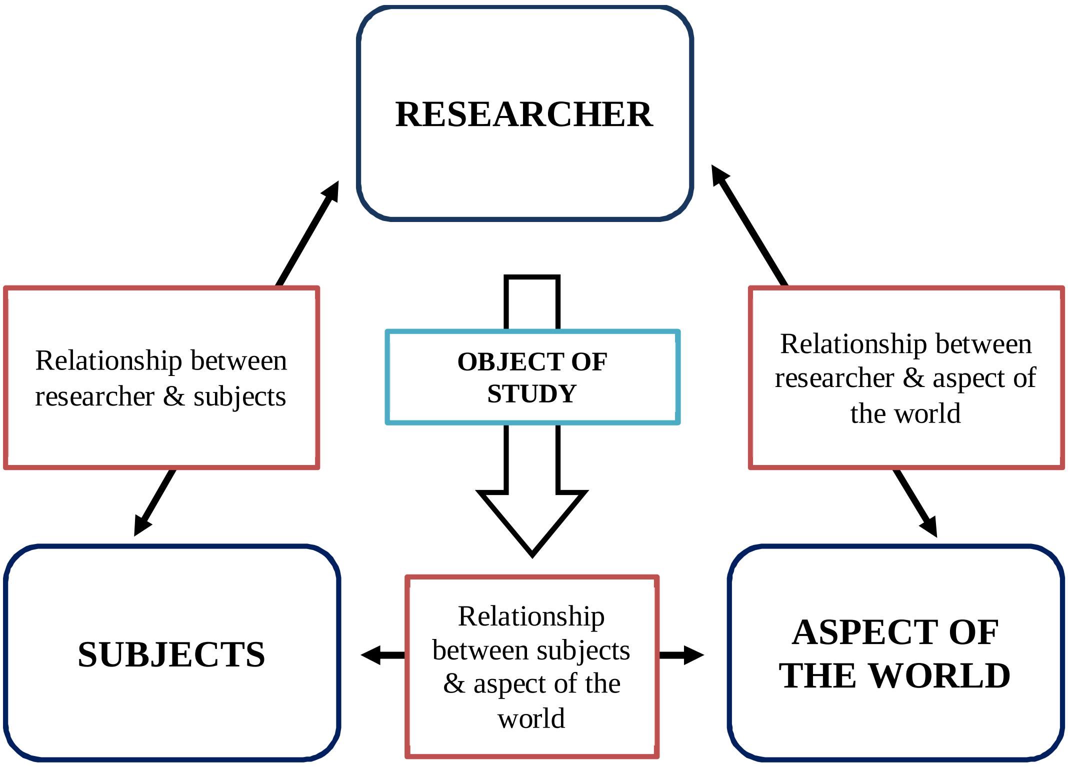



Figure 14: Focus of the phenomenographic research approach (Bowden and Green 2005, p. 13)

In phenomenography, ontology and epistemology are interdependent. The concept underpinning phenomenography is that thinking and experience are inseparable. Knowledge is neither external nor internal to individuals; rather, it is assumed to be gained through individuals' experience of situations in which the phenomenon is present. Through this experience, individuals have social and intellectual experiences of the phenomenon, where they gain their own understanding of it, as well as experiencing the understanding of other individuals (Marton and Booth 1997).

Phenomenographic researchers focus on individuals' consciousness of reality, that is, on ontological issues, as well as their expression of reality, that is, on epistemological issues. Such researchers do not take a first-order perspective and attempt to describe what reality is like; instead, they take a second-order perspective and focus on how it is experienced and described by individuals experiencing the phenomenon (Svensson 1997, Yates *et al.* 2012). Figure 15 describes how phenomenography differs from other research approaches. This study aimed to describe antibiotics prescribing, that is, the phenomenon, by GPs, that is, the subject, for elderly patients with UTIs visiting primary care, that is, the natural setting or context.


Figure 15: Point of departure between phenomenography and other research approaches (Trigwell 2006, p. 369)

#### *3.2.1.2.1.3 Sample Size*

In qualitative research, sample size can be a challenging concept (Patton 2002). The number of participants needed is different for qualitative research than for quantitative research since the generalisability of the findings of qualitative research is concept based, rather than numerically based as in quantitative research. In qualitative research, adequate sample size is achieved when no new themes emerge from subsequent participants' interviews, that is, data saturation has been reached, or when the capacity of the researcher to hold the evolving analysis in their mind has reached its limit (Ayres 2007).

In qualitative research, the sampling techniques used are either non-probability purposive, that is, the researcher makes the decision about the candidate to be included in the research based on several criteria including the candidate's knowledge of the research subject and their specialisation or capacity and willingness to participate in and answer the research questions (Jupp 2006), or theory based, that is, participants are chosen for inclusion to expand, confirm or endeavour to disconfirm a developing theory (Ayres 2007).

#### *3.2.1.2.1.4 Data Collection Methods*

Different methods of data collection are used in phenomenography such as asking participants to complete questionnaires or recording videos. However, interviews constitute the major method of data collection, since there is a necessity to understand the participants' worlds (Marton 1986, Maykut and Morehouse 1994, Marton and Booth 1997). This is evident from the use of interviewing as the primary method for data collection in several phenomenographic studies (Marton 1986, Dall'Alba and Hasselgren 1996, Ashworth and Lucas 2000). The main reason for this practice is its ability to capture concepts and beliefs and retrieve rich-content information about participants' ways of experiencing particular phenomena (Limberg 2000, Åkerlind 2005, Bowden and Green 2005, Stenfors-Hayes *et al.* 2013).

In qualitative research, interviewing is not just a casual conversation process, it is an interaction between the researcher and the participant or a group of participants with a predetermined subject to serve research objectives (Maykut and Morehouse 1994, Given

2008). Thus, it differs from other typical versions of interviews, and proposes a reformulation of the process:

> *'At its heart is the proposition that an interview is a form of discourse. Its particular features reflect the distinctive structure and aims of interviewing, namely, that it is discourse shaped and organised by asking and answering questions. An interview is a joint product of what interviewees and interviewers talk about together and how they talk with each other. The record of an interview that we researchers make and then use in our work of analysis and interpretation is a representation of that talk'* (Mishler 1986, p. vii).

In qualitative research, there are three main types of interview: structured, semi-structured and unstructured (Gill *et al.* 2008, Ryan *et al.* 2009). In structured interviews, pre-set questions are put to the participants with little or no difference and without follow-up questions to responses that might require additional explanation. They are efficient in terms of time, less biased and easier to code and analysed; however, they are of little benefit when in-depth information is required (May 1991, Ryan *et al.* 2009, Doody and Noonan 2013). At the opposite end of the scale, unstructured interviews do not use any pre-set designs, thoughts or questions and are usually conducted with little or no organisation making them flexible and rich in terms of data generation. Since they are none-directive, they can be time-consuming, difficult to manage and lack preconceived thoughts, theories or questions which may confuse the participants (May 1991, Ryan *et al.* 2009, Doody and Noonan 2013).

Semi-structured interviews, also known as non-standardised interviews, have a certain level of structure and flexibility since they allow the researcher to change the order of the questions, reformulate or rephrase questions to gain better understanding and clarification (Hallberg 2008). Moreover, they have the advantage of collecting detailed and complex data when in-depth information is needed (Kvale 1996, Patton 2002). Semi-structured interviews depend on a pre-set interview topic guide containing open-ended questions or issues to be discussed and explored with the participants. The pre-set interview topic guide ensures that the same basic lines of enquiry are followed up with each participant yet provides the interviewer with the chance to ask additional questions, using (Hawkings *et al.* 2008):

- probes, that is, open-ended questions that allow the researcher to gain a deeper exploration of a particular idea, perception or concept. These are used to rephrase questions whenever the participant is unable to provide an answer or reaction and/or to allow further exploration of an answer the participant has given during the interview process; and

- prompts, which provide participants with several response options following a question. Their aim is to trigger the participant's memory and to draw out ideas, thoughts or concepts that the participant may have been initially reluctant or hesitant to share. They can be used to enable participants to respond to questions they were unable to answer previously.

Additionally, both probes and prompts allow the researcher to discover or elaborate on information that seems important to the participants but that may not have been considered by the research team members during the topic guide development (Hawkings *et al.* 2008). Therefore, the researcher is free to direct the conversation within a particular topic, to rephrase questions spontaneously and to establish a conversational style, while keeping within the focus of the particular pre-set subject (Kvale 1996, Patton 2002).

In healthcare qualitative research, semi-structured interviews are the most widely used type as they provide participants with some guidance on the study or research topic, which many find helpful (Pope and Mays 2006, Ryan *et al.* 2009). Thus, for this PhD research, which requires the gathering of in-depth and complex information, qualitative, semi-structured, descriptive, single, face-to-face, one-to-one interviews were the best method of collecting data from recruited participants.

#### *3.2.1.2.1.5 Triangulation*

*'Triangulation'* describes the process of combining different study groups, methods, temporal and local settings, and different theoretical perspectives in dealing with a phenomenon. As a strategy, triangulation aims to promote and improve the quality of qualitative research (Flick 2009). In qualitative research, there are five types of triangulation that can be used, namely (Guion *et al.* 2001):

1. data triangulation;
2. methodological triangulation;
3. investigator triangulation;
4. theory triangulation; and
5. environmental triangulation.

Triangulation can have several advantages in qualitative research such as increasing data confidence, enabling creative and innovative understanding of phenomena, allowing comparison of research paradigms, challenging theories, revealing and recognising unique findings and outcomes, and providing clearer understanding of problems. It can also have many disadvantages, though, such as being resource- and time-consuming, and resulting in conflicts because of theoretical frameworks, researchers' biases and lack of understanding about why triangulation strategies were used (Thurmond 2001).

Phenomenography typically uses one source of data and one round of data collection only, and even several external members are generally not regarded as an appropriate validity check for this research approach. As a substitute for data triangulation and to ensure quality, strict adherence to the data within the interview transcripts is needed (Green 2002).

#### *3.2.1.2.1.6 Qualitative Data Analysis*

There is no singularly appropriate method of qualitative data analysis although there is general agreement that analysis is an ongoing, iterative process that begins in the early stages of data collection and continues throughout the research (Bradley *et al.* 2007). Methods of data analysis must be guided by the research's philosophical or theoretical assumptions of qualitative enquiry, epistemological position, research questions and methods of data collection (Miles and Huberman 1994). Qualitative data can be analysed either (Pope *et al.* 2006):

- inductively, which involves analysing data with little or no predetermined theory, structure or framework and uses the actual data themselves to derive the structure of analysis. This approach is useful when little or nothing is known about the study phenomenon; or

- deductively, using a structured or predetermined framework. This approach is useful when the researcher is aware of probable participant responses.

Two methods of analysis were used for this research: phenomenographic analysis and thematic analysis. The phenomenographic analysis uses mapping process, which is differentiated from the type of cataloguing process common in most qualitative analysis methods (Bowden and Green 2005). Furthermore, the data should be analysed and discussed from a second-order perspective that described how the phenomenon was viewed and understood by the participants rather than how it was understood by the researcher (Sjöström and Dahlgren 2002). Additionally, it analyses the range of meanings within a group, as a group, not the range of meanings for each individual within the group. This is misunderstood by some researchers (Marton and Booth 1997). The phenomenographic analysis process consists of a seven-step approach. Figure 16 illustrates the process which was proposed by (Dahlgren and Fallsberg 1991) for data analysis.

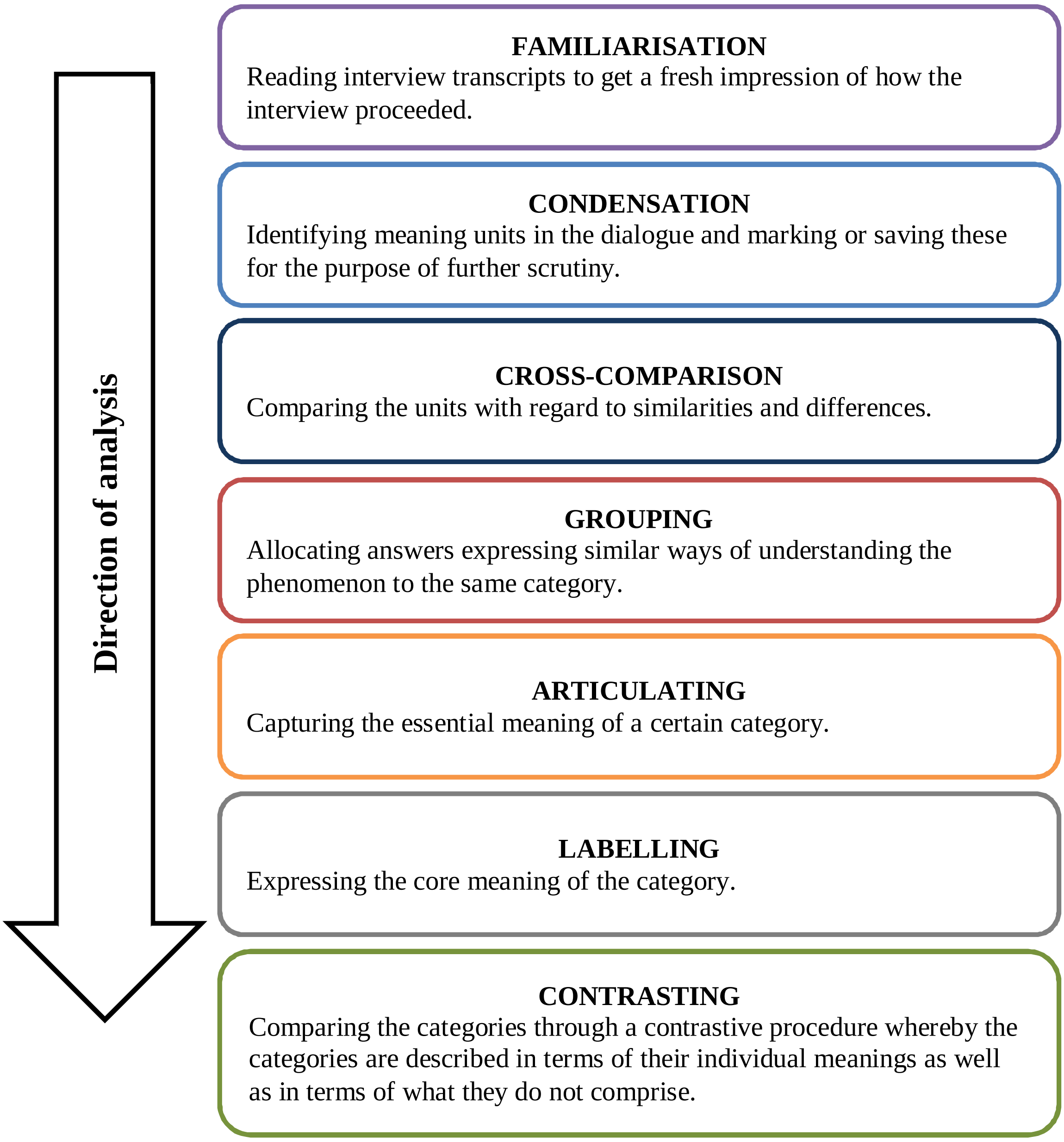



Figure 16: Seven-step process to phenomenological data analysis (Dahlgren and Fallsberg 1991, p. 152)

The outcomes of the phenomenographic data analysis are presented as categories of description and outcome space. Categories of description represent how a group of participants collectively experienced a specific phenomenon in its context (Åkerlind 2005). Owing to the nature of phenomenography, the categories of description do not fit into predetermined categories but, rather, emerge from the data themselves (Bruce 1994). Categories further presented using two components to establish the internal relationship: the subject–object relationship, which is established through a referential component, and a structural component (Limberg 2000). The referential component, that is, meaning, consisting of selected participants' statements from the interview transcripts to reveal the richness of the participants' conceptions. The structural component consisting of internal and external horizons. The internal horizon referred to the participants' focus point when they experienced or addressed the phenomenon, while the external horizon related to how component parts of the phenomenon are understood and are related to each other (Barnard *et al.* 1999, p. 216).

Outcome space is a graphical, hierarchical presentation of findings that consists of a related set of a finite number of categories of description that collectively express the variety of ways in which the phenomenon under study is experienced by a group of individuals in a given context, that is, the real world (Åkerlind 2005). The resulting outcome space is arranged so that more complex categories are placed above less complex categories (Marton and Booth 1997). Marton and Booth (1997) addressed three important criteria for determining the quality of phenomenographic outcome spaces (Marton and Booth 1997):

1. Each category reveals a unique aspect of how a phenomenon is understood.
2. Categories are connected in a hierarchical structure with relationships.
3. There is a limited number of outcomes, that is, a set few categories.

The second method is thematic analysis, which is independent, qualitative and descriptive and is mainly used to identify, analyse and report patterns, that is, themes, within data in nuanced and rich details (Braun and Clarke 2006, p. 79). Thematic analysis is appropriate for qualitative questions such as 'What are the concerns?' or 'What reasons do people have?'. The philosophical assumption for thematic analysis is based mainly on what is known as the *'factist'* perspective, which assumes that the reality regarding a specific attitude or behaviour exhibited by participants is indexed somewhere within the data, which are more or less accurate and truthful (Vaismoradi *et al.* 2013). Thematic analysis consists of a six-step approach. Figure 21 illustrates the process which was proposed by (Braun and Clarke 2006) for data analysis.

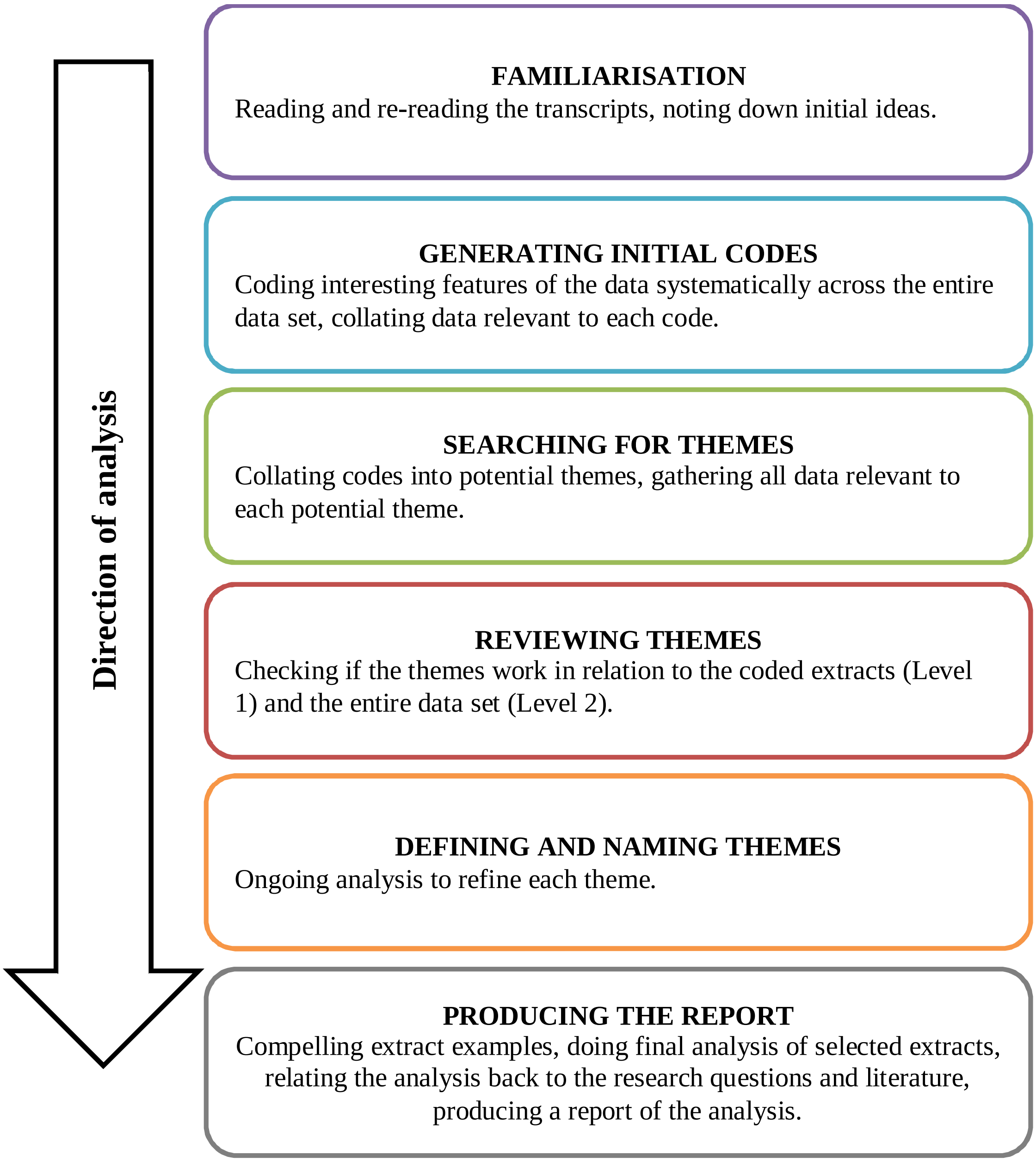



Figure 17: Six-steps processes for thematic data analysis (Braun and Clarke 2006, p. 87)

The outcomes of the thematic data analysis are presented as themes. A theme can be described as a coherent integration of the disparate pieces of data that constitute the findings (Vaismoradi *et al.* 2013). Themes capture important pieces of data that are relevent to the research question and represent some level of response pattern or meaning within the data set (Braun and Clarke 2006).

### *3.2.1.2.1.7 Trustworthiness (Rigour) in Qualitative Research*

Qualitative research is frequently criticised for its lack of scientific rigour. Such judgements stem from ideals and criteria suitable for a hypothetico-deductive model such as internal validity, reliability, generalisation and objectivity and as in quantitative research. Therefore, establishing rigour or trustworthiness is crucial in all qualitative research (Guba and Lincoln 1992, Hamberg *et al.* 1994). The concept of trustworthiness can bring qualities to qualitative research by applying four commonly used criteria (Figure 18): 1) credibility, that is, a quality assessment of whether the data convincingly describe the phenomenon under investigation (Lincoln and Guba 1985, Ritchie *et al.* 2014); 2) transferability, which refers to whether the descriptions and interpretations in the study are useful in other contexts (Lincoln and Guba 1986, Guba and Lincoln 1992); 3) dependability, which is a concept of consistency of the findings when the research is replicated and repeated in the same context, using the same method and the same participants (Lincoln and Guba 1985, Ritchie *et al.* 2014); and 4) confirmability, which is concerned with ensuring objectivity of word, that is, neutrality, and control of researcher bias (Lincoln and Guba 1985, Ritchie *et al.* 2014).

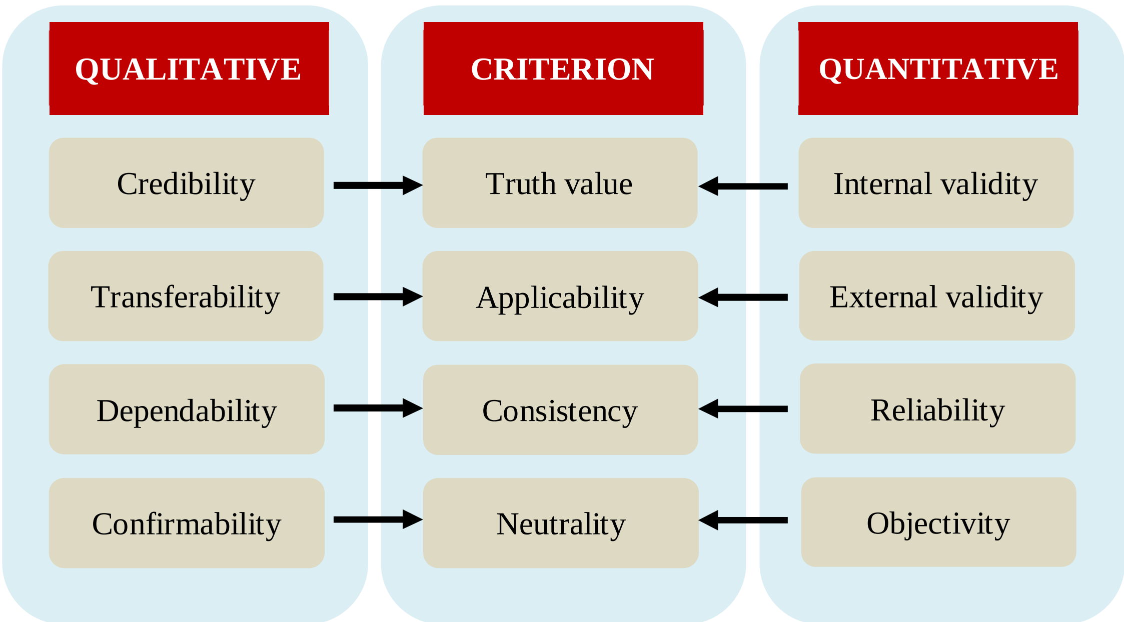



Figure 18: Indicators of scientific trustworthiness in qualitative research (Hamberg *et al.* 1994, p. 178)

No qualitative research, regardless of the method used, can provide findings that are universally applicable (Lincoln and Guba 1985, Mays and Pope 2000). In qualitative research, generalisability is concerned with the extent to which research findings can be relevant beyond the setting and context in which they were generated, that is, outside the sample in which the research was conducted (Lincoln and Guba 1985, Mays and Pope 2000). Qualitative researchers such as Lincoln, Guba, Ritchie and Lewis suggested that qualitative research's external validity can be strengthened by providing a thick description, that is, a comprehensive description and details, of the research design, method and data interpretation process to allow other researchers to confirm that the conclusions reached hold validity, assess the trustworthiness of the findings and evaluate the research limitations (Lincoln and Guba 1985, Ritchie *et al.* 2014).

## 3.3 Methods

### 3.3.1 Quantitative Study: Drug Utilisation Review of Antibiotics Prescribed by GPs for Elderly Patients with UTIs in a Primary Care Setting

#### 3.3.1.1 Study Design, Duration and Data Source

This study was a quantitative, retrospective, observational, cross-sectional drug utilisation study. It was designed to identify antibiotics prescribing patterns in addition to auditing and quantifying any inappropriate prescribing if present based on published good practice points (SAPG 2013). Patients' data were retrieved from a database for a 36-month period from 1 January 2010 to 31 December 2012 as in other research (Wrigley *et al.* 2002, Ki *et al.* 2004, Kahan *et al.* 2005, Galatti *et al.* 2006, Czaja *et al.* 2007, Petersen and Hayward 2007a, Taur and Smith 2007, Haasum *et al.* 2013). The study used data from the UK IMS-DA database as a source of patients' diagnosis and prescriptions data. At the time of this study in 2013, the database contained anonymised patient records from 135 general practices distributed all over the UK.

The reason for choosing retrospective drug utilisation was that it was recognised for its efficiency in addressing and describing drug prescribing patterns and problems, that is, auditing. Furthermore, it could lead to planning for future interventions intended to improve prescribing behaviour in addition to being inexpensive, quick and easy to perform and requiring only the use of routinely accessible data. The main disadvantages of this design are the limited number of variables available for analysis and there being more potential for bias and confounding than in other designs. However, the bias and cofounding in this design can be overcome by adhering to a well-structured design (Folke and Donald 2003, Shalini *et al.* 2010).

The IMS-DA was selected as data source because it is large and population based, that is, longitudinal, with high quality and validity. Furthermore, IMS-DA is unique, being the only database available that includes and combines all information on GPs, patients, diagnoses and courses of therapy relevant to the decision-making process (Becher *et al.* 2009). Additionally, IMS-DA was used to set the scene and to quantify the magnitude of inappropriate antibiotic prescribing if present. Moreover, an IMS-DA access licence was available through academic collaboration.

#### 3.3.1.2 Study Population

The study was designed to include all patients registered in the IMS-DA database aged 65 and older, coded by GPs, having had at least one code of UTI diagnosis, event or problem and having received antibiotic prescription(s) in the period from 1 January 2010 to 31 December 2012.

#### 3.3.1.3 Data Codes

Study diagnosis codes for UTIs were selected from the Read Codes dictionary (Appendix 5). These codes were listed on a Microsoft (MS) Excel® 2007 spreadsheet (Microsoft® Corporation. Released in 2007. USA) containing definitions and descriptions for all the codes found and used in IMS-DA by GPs during the process of data entry into the surgery computer system. All the selected codes were sent to a GP for validation before the process of data extraction was undertaken. After the codes were validated, a new MS Excel® spreadsheet was generated with all the approved codes for UTI diagnosis that would be included in the study.

#### 3.3.1.4 Data Extraction

The validated diagnosis codes list was used to extract patient details from IMS-DA with the help of a well-trained and experienced specialist in the field of pharmacoepidemiology and IMS-DA data from University College London (UCL), School of Pharmacy. A complete list of patient information extracted from the IMS-DA database for this study can be found in Appendix 6. Retrieved data were separated into several text files: a prevalence text file, an events text file, a problems text file and an antibiotic therapy text file (using E*ph*MRA AT classifications J01: Systemic Antibacterial Agents and G04:

Urinary Anti-Infective Agents and Antiseptics). For details of the AT codes of extracted antibiotics, see Appendix 7.

### 3.3.1.5 Data Reviewing and Cleansing

All text files were imported to MS Excel® as spreadsheets. Both events and problems files were combined in one spreadsheet and labelled as the UTI problems master file. Data were revised and cleaned by checking for any missing or unusual values and in-complete or bad entries, if present, before data were processed. No missing values or bad entries were detected during the review process.

### 3.3.1.6 Searching for Duplicate Data

The UTI problems master file was exported to IBM® SPSS® (Statistical Package for the Social Sciences) Version 21.0 software (IBM® Corporation. Released in 2012. IBM® SPSS® Statistics for Windows, Version 21.0. Armonk, NY: IBM® Corporation) for comparing practice identifier, patient identifier, diagnosis and date. Searching for duplicate cases between problems and events in the UTI problems master file was performed and any duplicate cases were excluded from the data. The search process successfully identified 25 duplicate cases. A decision was made to delete these cases to avoid any miscalculation when performing the statistical analysis. A new SPSS® file was created and saved as the UTIs final problems file.

### 3.3.1.7 Antibiotic Therapy and Data Linking

The antibiotic therapy file was imported to IBM® SPSS® 21.0 software. Data linking between antibiotic therapy and the UTIs final problems file was performed. Each patient was linked to his or her antibiotic therapy through matching several variables including practice identifier, patient identifier, date, age and gender to increase matching accuracy. Figure 19 illustrates the process of matching variables between the two files. A new SPSS® file was created and saved as the patients' data linked file. The saved file was used for computing, recoding and analysis.

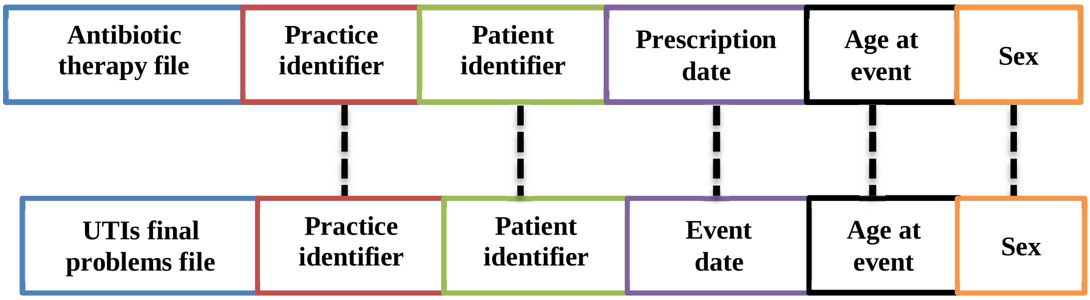



Figure 19: The process and variables used for data linking between files

### 3.3.1.8 Computing and Recoding Variables

Old variables from patients' data were recoded into new variables. The recoded variables were age, diagnosis, duration and date, as follows:

1. Age was recoded into three major groups: 65–74, 75–84, and 85 and older – to match some of the age groups published in the literature (Eriksson *et al.* 2010, Caljouw *et al.* 2011) and to make comparison between results feasible in terms of prevalence.

2. Diagnosis Read Code descriptions were recoded into four major groups,[24] to match the diagnosis and therapy recommendations:

   2.1. upper UTIs including pyelonephritis;
   2.2. lower UTIs including all types of cystitis;
   2.3. urinary tract infections including all diagnoses entered by GPs as urinary tract infection or urinary tract infection unspecified site; and
   2.4. others, containing any diagnosis other than those previously listed.

   More details about the different diagnoses under each of the four categories can be found in Appendix 8.

3. Duration was recoded into five groups: three days, seven days, 10–14 days, 28 days and others – to make it easier to compare it with the recommended therapy duration for different diagnoses.

4. Date as a quantitative variable was recoded into three major years – 2010, 2011 and 2012, according to patients' date of visit – to make it possible to compare patterns and trends among the years.

[24] All categories were validated by an external expert GP.

#### 3.3.1.9 Antibiotic Adherence to Good Prescribing Points

The decision aid document for the diagnosis and management of suspected urinary tract infection (UTI) in older people[25] was used to audit and compare the appropriateness of antibiotic drugs and durations of therapy. The criteria used to label antibiotics as inappropriate were the use of:

- antibiotic choice other than the recommended one;
- broad-spectrum antibiotics for UTIs other than recommended;
- antibiotics for durations other than recommended for treatment or prophylaxis; and
- doses of antibiotics other than those recommended.

#### 3.3.1.10 Statistical Analysis

Statistics in DUR are mainly descriptive in nature. Provision of certain information – such as epidemiologic parameters, that is, prevalence; degree of consumption, that is, number of prescriptions; drug prescription profiles considering different ages and genders – appears to be essential in DUR studies (Hallas 2005, Sequi *et al.* 2013). Descriptive statistics were performed on retrieved data to calculate means, standard deviation (SD) and distributions of demographics. This analysis was used to summarise, organise, graph and describe data (Kier 2011). Frequencies, that is, percentages, of patients' visits, diagnoses, and choice and duration of antibiotics prescribed were calculated by dividing each variable numerator by the relevant denominator and multiplying it by a hundred.

In this research, annual prevalence was defined as the number of patients with at least one antibiotic prescription for UTI during the year of investigation divided by the total number of patient-years, which in this particular case is 65 years and older, in the same year. Patient-years were defined as the sum of the number of years contributed by each patient at risk of being prescribed an antibiotic for UTI during the study period in the study population, namely, elderly patients aged 65 or older. In order to calculate patient-years,

[25] Although these recommendations were published in 2013, that is, they are newer than the used data, they were originally summarised from other old guidelines that were published in 2010 or earlier. Further, although 'non-adherence' usually reflects prescribing according to previously established recommendations, in this research it was used to describe any pattern of prescribing that was not in line with the 2013 good practice points.

the censoring date for each individual patient needed to be determined as some patients may have entered or left the clinic at various points in time owing to a number of reasons such as death or moving to another surgery in another catchment area that is not included in the database. Patients were eligible for inclusion in the study between their respective left-censoring and right-censoring dates in the database, that is, not all elderly patients were included in the prevalence calculation throughout the whole study period. The left-censoring date is the study start date, or the patient registration date, or the surgery up-to-standard date. The right-censoring date is the date data ceased to be contributed to the database, that is, when patients left, or moved out of the practice to another surgery, or died, or the study end date was reached. The left-censoring and right-censoring dates were used to calculate the length of time each patient contributed data to the IMS-DA database during the study period. Figure 20 illustrates the process of data censoring in the IMS-DA database for this study. The annual prevalence for elderly patients with UTIs was calculated per 1,000 person-years for the years 2010, 2011 and 2012 by dividing the numerator (registered cases of UTI per age) by the relevant denominator (total number of patients-years of the same age) for the same period of time multiplied by 1,000 as in (Hsia *et al.* 2010, Schnabel *et al.* 2015). The reason for using this unit for prevalence reporting in this research was its ability to accommodate patients coming into and leaving during the study period to provide more accurate figure; however, using this unit might result in a lower prevalence compared with prevalence from other literature.

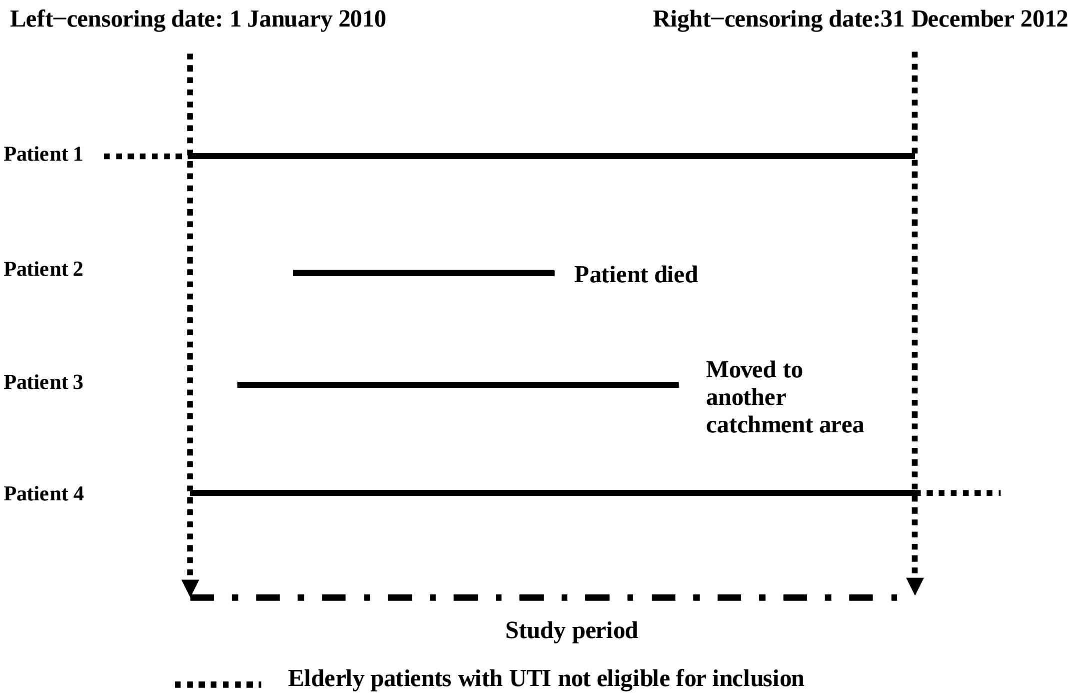



Figure 20: The process of data censoring in the IMS-DA database

Overcoming the influence of age and sex that may confound comparison of UTI prevalence was done using the standardisation method, that is, adjustment in the calculation. Age and age–sex standardised prevalence rates were calculated using the direct standardisation method owing to the nature of the study data (Tripepi *et al.* 2010). As a standard population for standardisation calculation, the UK 2012-based National Population Projections by the Office for National Statistics (ONS) were used (ONS 2013). To ensure the reliability of the prevalence estimate, a 95% confidence interval (CI) was calculated for each prevalence rate. The CI is a range of values calculated by statistical methods that includes the desired true parameter with a probability defined in advance. The 95% CI means that the confidence interval covers the true value in 95 of 100 studies performed (du Prel *et al.* 2009). Student's t-test was used to compare overall mean between male and female and per year as well. One way analysis of variance (ANOVA) test was used to assess the significant in prevalence over the study period using year as the dependent factor and prevalence as independent factor.

Patterns of antibiotic use were defined as the extent and profiles of antibiotic use and the trends in antibiotic use over time (Birkett *et al.* 2003). Antibiotic patterns and trends were identified for the most commonly prescribed antibiotics per annum and throughout the period of the study by dividing the numerator that represents the total amount for each antibiotic prescribed by the relevant denominator, which in this case was the total number of whole antibiotics prescribed for a certain period or for the whole period. To examine if changes in antibiotic prescribing over the study period were significant, Chi-square ($\chi^2$) test was used. GPs' adherence to good practice points for prescribing antibiotics for UTIs was assessed through cross-tabulation of diagnosis and gender for the overall study period then a percentage was calculated for each antibiotic compared with the decision aid document points using IBM® SPSS®.

Inferential statistics were also calculated to determine the likelihood that a conclusion, based on the data from a sample, was true and represented the population studied (Kier 2011). The Chi-square test for categorical variables and the Student's t-test for continuous variables were used when appropriate to compare group means and to detect the statistical significance of results (du Prel *et al.* 2010). A $p$-value of $< 0.05$ was considered to be statistically significant.

In this study, two external statisticians assisted in the performance of statistical analyses, confirming the suitability of the tests performed and the accuracy of the results obtained. All results were presented in the form of column charts, cross tables and line charts. All tables and figures were generated using MS Excel® 2007. Data analysis was carried out using IBM® SPSS® Version 21.0 software. Figure 21 illustrates the methodology steps followed in this study.

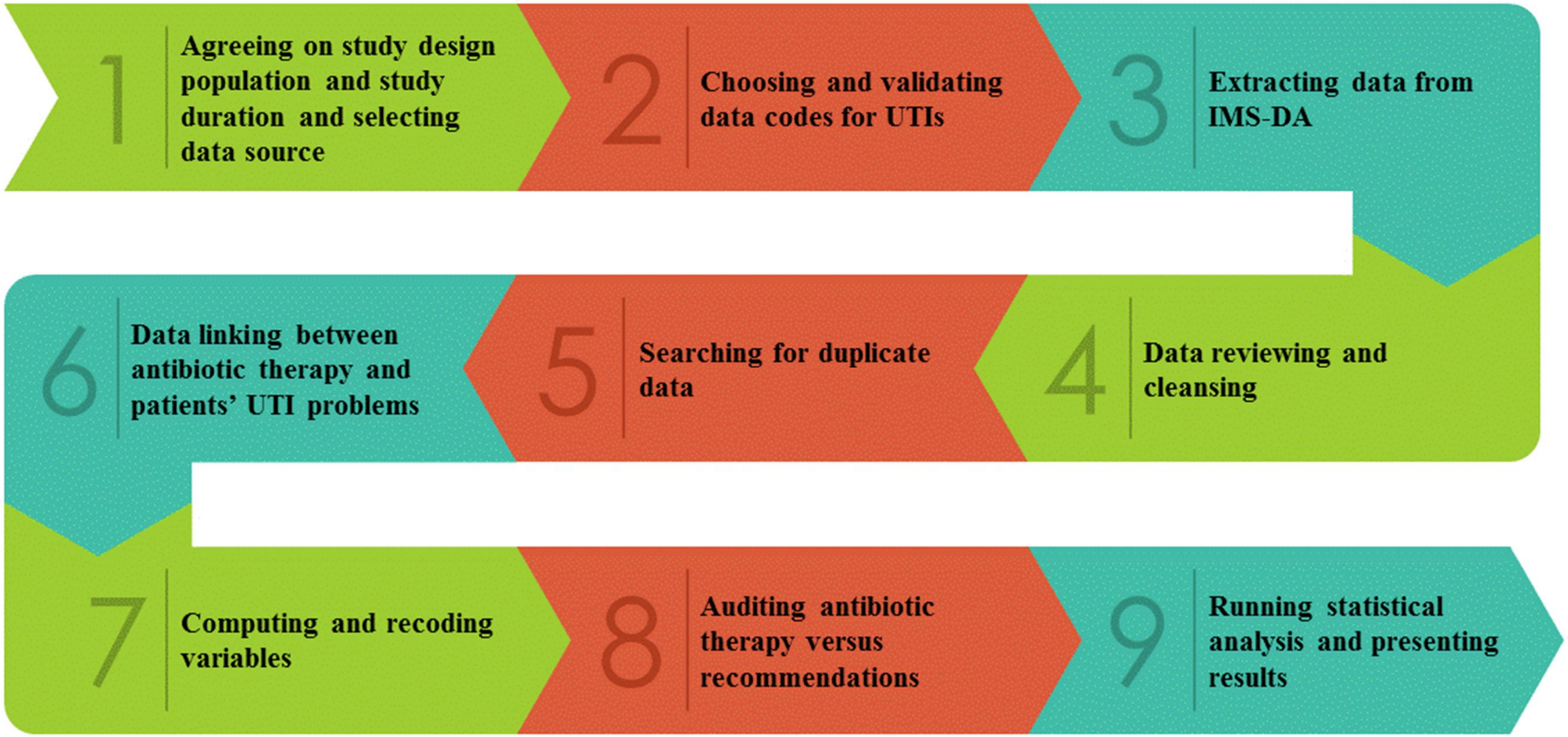



Figure 21: Summary of the methodology steps followed in DUR study

#### 3.3.1.11 Ethical Considerations

Before starting the study, an email was sent to the Research Ethics office at KCL to verify whether the study would need ethical approval or not. The response from the Research Ethics office indicated that the study did not require any ethical approval from KCL since the study uses only pre-existing, fully anonymised and non-sensitive data. Therefore, no ethical approval was needed to conduct the study (see Appendix 9). However, IMS Health requested submission of the research proposal via the Independent Scientific and Ethical Advisory Committee (ISEAC) form in addition to a payment to review the research protocol used and provide approval for publication. The form included all details of the research – study aim, objectives, detailed study protocols – in addition to references to obtain grants to use the databases and to publish and present the results of the study in the literature and at conferences. The committee revised the form and requested further clarification of some minor points. Final ISEAC approval was obtained from the committee in June 2014 (see Appendix 10).

### 3.3.2 Qualitative Study: Variations in GPs' Views and Perceptions about Prescribing Antibiotics for UTIs in Elderly Patients and Factors Influencing GPs' Antibiotics Prescribing for UTIs

#### 3.3.2.1 Rationale for Phenomenographic Research Design

To achieve the aim of the qualitative arm of research, it was highly important to explore how people perceive or understand a phenomenon or situation since people plan their actions according to their perceptions (Svensson 1997). Therefore, a phenomenographic approach was deemed to be appropriate because of its second order philosophical approach which is related to exploring variations in peoples' experiences of a particular phenomenon by studying their different views, concepts and thoughts about it (Marton 1986), which is one of the objectives of this research. Phenomenography assumes that experiences can differ not only between people but also within the same subject over time, because different aspects of a phenomenon are conceived within a framework in relation to a given context (Barnard *et al.* 1999). Accepting this fact, in addition to gaining knowledge about these different ways, allows researchers to understand:

> *'How the world appears to others, what the world is like, and what the world could be like'* (Marton and Booth 1997, p 13).

There is evidence, too, from previously published studies about the appropriateness of phenomenography for exploring variations in GPs' views about drug prescribing (Lundborg *et al.* 1999, Wahlstrom *et al.* 2001, Rahmner *et al.* 2009).

#### 3.3.2.2 Research Setting and Sampling Strategy and Sample Size

The qualitative study was designed to recruit any GP who works in the NHS or for an NHS partner surgery within Greater London, in the UK, to maximise the variation in capturing concepts and understanding. London was chosen for its convenience in terms of GPs travelling to take part in this research and for the cultural diversity of its GPs and patients, which might have an impact on the phenomenon of antibiotics prescribing.

The fundamentals that underpinned the recruitment strategy in this research were the adequacy and appropriateness of the recruited participants. Adequacy referred to sufficient relevant data being generated through the participants while appropriateness referred to selecting participants with relevant experience and knowledge to inform the research (Bassett 2004). Therefore, non-probability purposive sampling, also known as judgemental, selective or subjective sampling, was adopted as the sampling technique.

As this was PhD research, the anticipated sample size was determined to be between 10 and 20 GPs subject to the concept of data saturation (Fitzpatrick and Boulton 1994, Guest *et al.* 2006, Mason 2010). Sample sizes of up to 20 have enabled exploration of all the diverse ways of conceiving of a phenomenon within a group of participants in similar settings (Lundborg *et al.* 1999, Wahlstrom *et al.* 2001, Rahmner *et al.* 2009). Studies relevant to GPs' views on UTIs have used similar sample sizes, from 15 to 20 (Kuehlein *et al.* 2011, Bjorkman *et al.* 2013, Duane *et al.* 2016).

#### 3.3.2.3 Inclusion and Exclusion Criteria

In order to capture a variety of perceptions and views regarding GPs' antibiotics prescribing, the recruitment criteria were broadened purposefully to include any GP with a degree in medicine, working in any NHS or NHS partner GP surgery in Greater London as a part-time or full-time GP, regardless of age, gender, practice location, practice size, contract scheme, years of practice, level of experience and training qualifications in an attempt to maximise the variation and diversity within the recruited participants.

GPs working in private GP surgeries were excluded from the study because of workload and the socio-economic nature of the patients who visit these surgeries. Additionally, GPs working in university or college primary care centres or surgeries were excluded since these centres and surgeries are mostly concerned with treating students rather than elderly patients.

### 3.3.2.4 Participants' Recruitment

Candidate recruitment[26] was carried out between 19 November 2014 and 5 February 2015. Three recruitment approaches were used to increase the number of participants and awareness about the study. The first approach was through email communication, circulating research details and recruitment invitations through the assistance of the Primary Care Research Manager at Imperial College London, Department of Primary Care and Public Health. The circulated email included a brief research description, research inclusion and exclusion criteria, researcher's contact details and instructions for interested GPs to provide the researcher with details including age, gender, certificates, years of experience, practice site location and whether they worked in a private or NHS or NHS partner surgery. Instructions to contact the researcher directly for further enquires, if needed, were also provided. See Appendix 11.

The second approach was through social media (the GPs page on Facebook® includes more than 3,000 GPs practising within the UK (www.facebook.com/groups/tikosgpgroup)). A private message containing the research and recruitment invitation details was sent to all group members through one of the group administrators. The message included a brief research description, research inclusion and exclusion criteria, the researcher's contact details and instructions for interested GPs to provide the researcher with details including age, gender, certificates, years of experience, practice site location and whether they worked in a private or NHS or NHS partner surgery. Instructions to contact the researcher directly for further enquires, if needed, were also provided.

The final approach involved sending a direct email to medical training supervisors and medical training programme directors at several primary care surgeries. The email

[26] Refers to the process whereby the researcher identifies and invites (recruits) participants to join the study (Given 2008, p. 743).

included a brief research description, research inclusion and exclusion criteria, the researcher's contact details and instructions for interested GPs to provide the researcher with details including age, gender, certificates, years of experience, practice site location and whether they worked in a private or NHS or NHS partner surgery. Instructions to contact the researcher directly for further enquires, if needed, were also provided.

Any GP interested in participating in the research was screened for appropriateness against the inclusion and exclusion criteria, with a view to maximising the variation among interested GPs. All eligible GPs received a detailed invitation email asking them to select their preferred day, date, time and place. The invitation email included the research title, a brief explanation of the research, its aim and objectives, the estimated interview length, suggested dates and times, incentive provided to those who agreed to take part in the research and never to withdraw from the study and the researcher's contact details for further enquires, if needed (Appendix 12).

Once interview dates were confirmed, participating GPs were emailed interview details and a research information sheet. It provided comprehensive details about the research including a brief research description, and information about the interview process and participants' rights. It included the study title, an invitation paragraph, the purpose of the research, the reasons for invitation, an explanation of the interview process, the research withdrawal policy, the incentive, possible disadvantages and risks of taking part in the research, possible benefits of taking part in the research, participants' anonymity, participants' and data confidentiality, the plan for disseminating research results and the researcher's contact details for further enquires (Appendix 13). All selected GPs received a mobile text message and an email reminder that included the interview day, date, time and place 48 hours before the interview.

#### 3.3.2.5 Development of the Interview Topic Guide

The interview was directed by an interview topic guide that was prepared in advance to ensure that the same basic lines of enquiry were followed with all participating GPs (Appendix 14). The interview topic guide was developed and designed based on previously published relevant qualitative studies as suggested by (Bowden and Green 2005, Flick 2007). Since there was a lack of similar studies on UTIs in elderly patients in primary care, studies on children and adults and a variety of infections such as RTIs and general infectious diseases were used to develop the interview topic guide questions (Tonkin-Crine *et al.* 2011a, Brookes-Howell *et al.* 2012, Bjorkman *et al.* 2013, Mustafa *et al.* 2014). All questions were re-drafted several times by research team members to best fit the research aim, questions, population, setting and type of infection. The design of the interview topic guide questions was influenced by the search for qualitative variations in participants' conceptions and experience.

The interview topic guide questions were designed to be open-ended to capture in-depth information and to maximise variations and diversity in the ways in which GPs experience antibacterial prescribing with special emphasis on elderly patients with UTIs. Questions were written in neutral and clear language to allow GPs to structure their own conceptions, beliefs and experiences (Patton 2002). They were prepared in a style to encourage and motivate participants freely to express their views and perceptions according to how they experienced the world of antibiotics prescribing in general and in comparison with their colleagues (Bruce 1994). They were neither too many nor included too many details that had been determined in advance since the idea was for most of the questions to follow on from the GPs' previous answers (Ashworth and Lucas 1998). The interview topic guide was divided into two parts as shown in Figure 22.

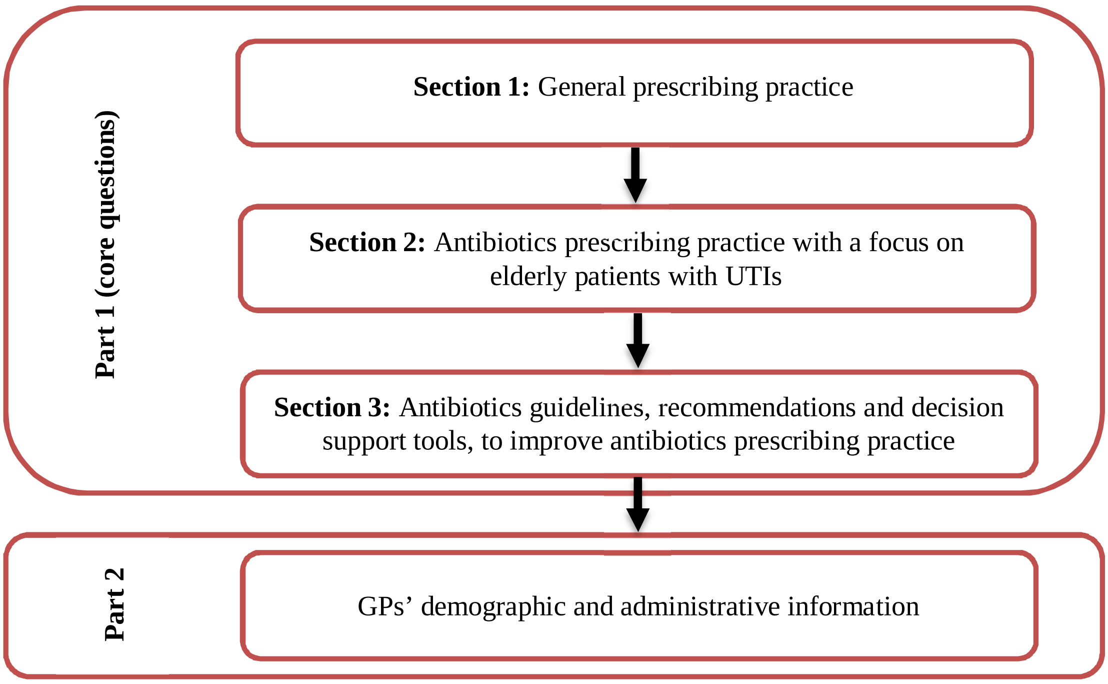



Figure 22: Summary of the interview guide main parts and the content of each part

The first part had the core questions and was further divided into three sections, each of which included questions relevant to a specific topic. The first section had introductory questions related to GPs' daily general practice, such as 'What are the most frequently prescribed classes of medication?' and 'What are the factors affecting GPs' prescribing practice and behaviour?'.

The second section related to antibiotics prescribing practice with the emphasis on elderly patients with UTIs. These were more specific, narrower questions related to antibiotics such as perceptions, problems, utilisation, prescribing, references, in addition to UTI drugs decision-making, variations in antibiotics prescribing among different ages of patients with UTIs, variations in antibacterial prescribing between elderly males and elderly females and factors affecting GPs' antibacterial prescribing practice and behaviour. These questions were developed to provide in-depth insight into how GPs in the UK approach elderly patients with UTIs in comparison with other age groups.

The third section related to antibacterial guidelines, recommendations and decision support tools, to improve antibacterial prescribing practice. These questions were developed to encourage GPs to express their personal experiences and thoughts about recommendations and guidelines in addition to decision support methods.

The second part of the interview questions focused on GPs' demographics and administrative information, including gender, age, practice site, country of study, qualifications, practice interest, number of years in practice, any experience outside the UK, working pattern, previous hospital experience, number of working days per week, average number of patients seen, examined and spoken to over the phone per day and average consultation length per patient. The reason for including all these details was to identify whether there was any interrelated pattern or relationship between these factors that might influence GPs' antibacterial prescribing perceptions.

#### 3.3.2.6 Piloting the Research

The phenomenographic literature emphasises the benefits of performing a number of small pilots prior to performing the main interviews (Dall'Alba and Hasselgren 1996). This practice strengthens the research outcomes, comprehension and clarity of the questions, and ensures that the data collection best captures the phenomenon under study (Bowden and Green 2005, Pulcini *et al.* 2011). Additional benefits include providing the researcher with a chance to practise and gain the necessary interviewing skills in terms of asking questions, prompts, probes and interacting with participants, as well as providing an average estimated interview length.

After the interview topic guide was revised five times by the research team members, both independently and together, it was further revised by four different clinical pharmacists with different qualifications (master's degree, doctor of pharmacy degree and doctor of philosophy degree). All necessary amendments and feedback resulting from the revisions was taken into consideration. A revised version of the interview topic guide was developed and tested in two pilot interviews. The first interview was with a practising GP and the second was with a prescribing consultant clinical pharmacist specialising in infectious diseases. The interview lengths were 50 minutes for the first interview and 67 minutes for the second. The pilot led to splitting one of the interview questions into four separate questions. No further amendments were suggested and a final version of the interview topic guide was developed. Neither of the pilot interviews was included in the qualitative sampling frame or the analysis. Figure 23 illustrates the phenomenographic research design and data collection approach followed in this research.

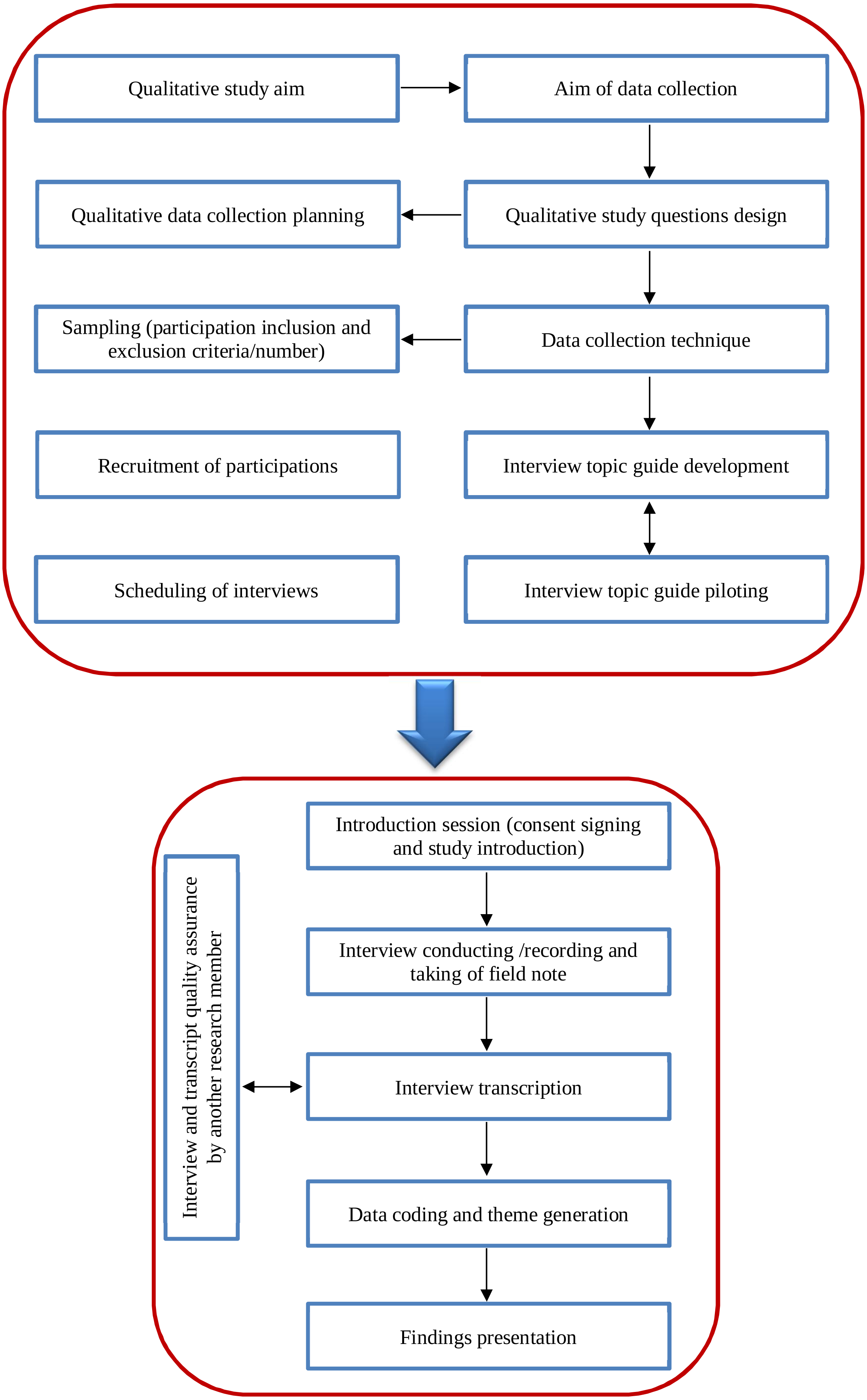



Figure 23: Systematic approach for the phenomenographic research design and data collection

### 3.3.2.7 Ethical Approval

The Research Ethics office at KCL advised that no ethical approval was needed for the study, since this type of research falls under service evaluation and audit. However, since the study involved GPs from the NHS, the KCL Research Ethics website provided instructions on how to contact the Health Research Authority (HRA) to check whether there was any need for ethical approval from the HRA research committee. An enquiry email was sent to HRA with a brief research description. HRA responded by advising use of the National Research Ethics Service (NRES) online decision tool. It stated that the outcome generated by the decision tool could be taken as an authoritative decision with no further confirmation required. It also suggested reading and following the HRA research guidelines before starting the study. The decision tool showed that the research did not require ethical approval (Appendix 15).

### 3.3.2.8 The Interviews Dates and Locations

Interviews were conducted between 7 January 2015 and 10 February 2015. All the 17 interviews were conducted in quiet rooms or similar places according to GPs' preference such as GPs' clinics, departmental meeting rooms, GPs' houses or study group rooms in KCL's Franklin-Wilkins Building library, 150 Stamford Street, London, UK.

### 3.3.2.9 Pre-interview Process

On interview days, all participant GPs were provided with a brief verbal explanation of the research and the interview process and invited to ask questions. They then asked to sign and date a consent form that provided all the information required to make an informed decision. All consent forms were dated and signed by the researcher as well. It consisted of 11 statements concerning the research, all written in simple, plain language and included the research title, an introductory paragraph, statements relating to the information sheet, participants' willingness to participate voluntarily, participants' anonymity, participants' and data confidentiality, the results dissemination plan, interview recording and use of quotes without using names for research results dissemination (Appendix 16). Each statement had to be ticked separately. All GPs were informed about their right to withdraw their data at any time, even after signing the consent form, without justifying their decision, as long as it was before 28 February 2015.

If a GP decided to withdraw from the research before that date, all his or her information, digitally recorded interview and collected data would be deleted and destroyed. Verbal confirmations from all GPs were obtained to digitally record interviews.

### 3.3.2.10 The Interview Recording

All interviews were digitally recorded for active listening and verbatim, word-for-word transcribing. To avoid any bias or confusion, terms used by GPs during interviews were used as they were. Interviews were digitally recorded using two different digital recorders. The first digital recorder was an Olympus® VN-712PC digital voice recorder and the second was the researcher's iPhone 5® device using the ALON Dictaphone® voice recording application (ALON Software Limited) Version 1.2. Both recording devices were tested during the two pilot interviews to check their reliability and quality of recording. The quality and clarity of the recorded interviews were excellent without detected noises. The reason for using two different devices was to have a back-up in case one device ran out of battery or a malfunction occurred. Olympus® digital recorder batteries were changed before each interview and the electricity charger was plugged into the iPhone 5® during all the interviews.

### 3.3.2.11 Interview Process

The interview process was sequential, with responses moving along the topic guide questions. Each interview began with the general introductory prescribing questions, to gain GPs' trust and make them feel at ease, and motivate them to answer the questions fully. As the interviews progressed, the questions explored antibiotics prescribing for UTIs in elderly patients in more depth, followed by guidelines and decision support tools and systems.

To reveal the GPs' ways of viewing antibiotics prescribing, the following techniques were used during the interviews to achieve the study objectives (Bruce 1994):

- encouraging reflection on experience (from your own experience) (Bruce 1994);
- asking for information about how the phenomenon appeared to the participants (in your opinion);
- confronting and pursuing areas of confusion (let me rephrase the question); and
- asking for explanation or more detail (can you elaborate more?).

Throughout all the interviews, generic probing and prompting questions were asked. A generic set of probes was used that had been published previously in the phenomenographic literature (Bowden and Walsh 2000). These included:

- Can you explain that further?
- Can you give me an example?
- What do you mean by that?
- Can you tell me more about that?
- Can you explain that in a different way?
- Is there anything else you would like to say about this?

**3.3.2.12 Taking Notes**

Notes were taken during the interviews, without distracting the participants. Notes included details that could not be captured by the digital recorder such as participants' non-verbal behaviour, tone and context. Notes were also taken of relevant conversations before and after the recorders were switched on, and of impressions formed about each interview as soon as possible after completing it. This approach was helpful in reviewing interview techniques in respect of ways of asking questions, as well as creating rapport with participants.

**3.3.2.13 Research Incentive**

As a token gesture, all GPs who took part in the interviews were awarded £100 in the form of an Amazon gift card. The incentive was given as a reimbursement for GPs' time lost to take part in the research. All gift cards were distributed after the end of the research with an appreciation email.

**3.3.2.14 Participants' Anonymity and Data Storage**

All GPs' information was anonymised by assigning each of the GPs a unique code (GPX) where (X) referred to the GP number in the research. All of these codes were kept separately from GPs' demographics and administrative details and encrypted by VeraCrypt® Version 66 for Windows® software (released by IDRIX on 30 December

2014, Paris, France). Furthermore, codes were kept strictly protected from any access except by research team members.

All digitally recorded interviews and information collected during the interviews was held on a password-locked encrypted computer. All GPs' consent forms and interview transcripts were locked in a filing cabinet in the researcher's office at the Institute of Pharmaceutical Science, KCL, Franklin-Wilkins Building, 150 Stamford Street, London, UK. All digitally recorded interviews and transcripts will be deleted and destroyed when the research is completed.

#### 3.3.2.15 Interview Transcription

All digitally recorded interviews were transcribed within two days using clean verbatim technique (Platt 2001, Patton 2002, Denzin and Lincoln 2011). It included the omission of certain words and utterances such as stutters, repetitions, false starts and most of the *'ums'* and *'ahs'* that would not affect the process of analysis. No attempts were made to correct the researcher's or the participants' sentence structure, grammatical mistakes, or use of colloquialisms. Three British English dictionaries were used to identify and understand the meaning of new or urban words: the Collins English Dictionary (Collins Dictionaries 2014), the Cambridge Essential English Dictionary (Cambridge University Press 2011) and the Urban Dictionary (Alexa Internet 2014). For quality assurance purposes, all transcripts were verified twice by the researcher versus the digitally recorded interviews and once by another research member (Dr Sue Jones (SJ)). Each revision was from a different recording device to assure the accuracy of interview transcription and word capture.

#### 3.3.2.16 Data Coding

In phenomenographic analysis, the processes of data coding and analysis should not be performed until all the interviews have been conducted (Bowden and Walsh 2000). In contrast, in thematic analysis, the process of data coding and analysis is ongoing and runs alongside the data collection process (Braun and Clarke 2006). The reason for keeping data coding and analysis in phenomenography until the end is that the data must be analysed as a whole because the aim of phenomenographic analysis is to explore the range of meanings within a group of individuals, as elaborated on earlier in this chapter.

In order to be familiar and understand the collected data, all recorded interviews were listened to twice and transcripts were read three times, all the while keeping the question in mind: 'What does this say about how GPs experience antibiotics prescribing when considering the elderly population?'. This technique ensured intense researcher engagement with the data at a deeper level, which helped in the ensuing data coding step. At this stage, the data was treated with an open mind, without any preconceived ideas about the phenomenon under investigation.

Codes are labels assigned to segments of transcripts such as words, sentences and paragraphs that facilitate the process of indexing or sorting key concepts while preserving the context in which these concepts occurred (Denzin and Lincoln 2011). The coding process used in this research consisted of a three-step approach that included development, finalisation and application of the code structure. All transcripts were coded inductively from the 'bottom up', because of the limited pre-existing work and theoretical frameworks. Sections of text, that is, quotes, were assigned to different labelled codes.

To facilitate the data coding and organisation of the interviews, NVivo® for Windows®, a computer software package developed to assist researchers in organising non-numerical or unstructured data, Version 10.0 (QSR International. Released in 2012) was used. A new project was created in NVivo® and saved under the name of GPs UTI Study. Each interview transcript word file was saved as Interview-X where X referred to the order of the interview. Each interview was linked to its participant's demographics and administrative data to facilitate the detection of interrelation if present. As there was a large volume of data transcripts, NVivio® was very useful in sorting, selecting, creating nodes for, comparing and grouping textual data from transcripts in a controlled and systematic manner (data coded under a topic heading and further coded into sub-topics). All codes were verified for meaning and consistency by the researcher and supervisors. See Appendix 17.

#### 3.3.2.17 Data Analysis Methods

Since this research was designed to explore the phenomenon of antibiotics prescribing in its natural setting, it was crucial to find a method of analysing the data that would allow exploration of the variations in participants' views and perceptions without imposing any pre-existing theory of what they might be. Furthermore, the method needed to allow identifying patterns in the data and instances of similarity and dissimilarity both within and between the participants' narratives. Additionally, the method had to discover unexpected findings, explore unique responses, give voice to the participants' conceptions, thoughts, and, if appropriate, interpret their responses in a way that could bring life to their narratives by richly describing the data (Sharma 2004, Forster 2013, Vaismoradi *et al.* 2013). Therefore, two different methods for data analysis were used: phenomenographic data analysis and thematic data analysis. Both techniques have many key advantages such as accessibility to less experienced researchers, flexibility, convenience of presenting findings, and ability to summarise key features and highlight similarities and differences across the data (Sharma 2004, Forster 2013, Vaismoradi *et al.* 2013).

Phenomenographic data analysis was employed in this study to discover and identify variations in GPs' experiencing of antibiotics prescribing for UTIs in elderly patients. A seven-step process proposed by Dahlgren and Fallsberg (1991) was adopted to perform the analysis. Thematic data analysis was employed to explore the factors influencing GPs' antibiotics prescribing. The thematic analysis was performed using a six-step process that was proposed by Braun and Clarke (2006).

Collected data were analysed by two researchers (HA and SJ) manually and independently. In order to harmonise the categories of descriptions and themes, mutual discussions between the two researchers were initiated to compare generated conceptions, categories and themes. The approach taken was not sequential, but was performed in an iterative manner, until the analysis was completed. The use of this method in analysis has been shown to be beneficial in generating a reasonable conclusion (Dahlgren and Fallsberg 1991, McCosker *et al.* 2004). In this research, all data coding and research analyses were double-checked by an external expert.

The core findings from the analysis were presented in several formats. The first was tables summarising participants' demographics and administrative information as well as themes and sub-themes generated from the thematic analysis. The second format included the findings from the phenomenographic analysis of the interview textual data, which were presented in the form of categories of description and outcome space and figures. The third format was extracts, that is, quotes, which supported the findings from the phenomenographic and thematic analyses. The term '*quote*' in this thesis refers to a segment of interview textual data of any length that was assigned a specific code. A quote may consist of a few words only, a sentence, a paragraph or even multiple lines of interview conversation (Creswell 2007). Each quote was identified by the abbreviation GP, which stands for general practitioner, followed by a number that described the GP's place within the interviews sequence as well as their age, gender and years of practice. The relevant code was positioned after each quote.

## 3.4 Summary

This chapter has reviewed the theoretical background to the methodological approaches employed in this thesis in addition to describing the precise methodologies followed to achieve the thesis' aim and research questions. The next chapter describes the research key results and findings.

# Chapter 4 Drug Utilisation Review of Antibiotics Prescribed by GPs for Elderly Patients with UTIs

## 4.1 Introduction

This chapter the key results and discussion about GPs' prescribing of antibiotics for elderly patients with UTIs who visited GP surgeries, from quantitative perspectives using DUR as methodological approach.

## 4.2 Results

The first section of this chapter presents the key results from the DUR study including details of patients' visits, the antibiotics prescribed and the number of GP surgeries that were included in the analysis during the study period. Patients' demographic information, the prevalence of UTIs and the adjusted prevalence for the study period are presented after that. The results regarding frequencies of patients' visits including individual patients' visits and patients' diagnoses are presented and categorised per patients' gender and age groups. Antibiotics prescribed and treatment durations are presented with regard to UTI type, years and patients' age groups. Finally, results of GPs' antibiotics prescribing and their adherence to UTIs good practice points were cross tabulated by diagnosis and gender.

### 4.2.1 Number of Extracted Records, Elderly Patients, Patients' Visits, Antibiotics Prescriptions and General Practices

Table 20: Summary of the number of visits, antibiotics prescriptions and GP surgeries that recorded data for elderly patients with UTIs during the study period

| **Year** | **UTI events visits** | | **Antibiotics prescriptions** | | **GP Surgeries** [27] | |
|---|---|---|---|---|---|---|
| | **N** | **%** | **N** | **%** | **N** | **%** |
| **2010** | 28,056 | 36.3 | 13,551 | 35.8 | 134 | 99.3 |
| **2011** | 25,946 | 33.6 | 12,849 | 34.0 | 126 | 93.3 |
| **2012** | 23,288 | 30.1 | 11,415 | 30.2 | 113 | 83.7 |
| **Total** | **77,290** | **100** | **37,815** | **100** | | |

During the time of commencing of this study, the IMS-DA included more than two million anonymous patient records and over 95 million prescriptions from about 135 GP

[27] Total number of GP surgeries included in IMS-DA for the period from 2010-2012 was 135 surgeries.

surgeries from all over the UK. Results shown in Table 20 summarise the number of elderly UTI visits, issued antibiotics prescriptions and GP surgeries from which visits and prescriptions were retrieved over the study period, (1 January 2010 to 31 December 2012). Results from data analysis identified events and prescriptions recorded by 134 different GP surgeries. These surgeries recorded a total of 77,290 UTI visits by 21,150 elderly patients, of whom (N = 16,375; 77.42%) received at least one antibiotic prescription per visit over the study period. The total number of issued antibiotics prescriptions for UTIs during the study period was 37,815. As the table shows, there was a consistent reduction in UTI events visits and antibiotics prescriptions. The highest numbers of visits and prescriptions were recorded in 2010 with (N = 28,056; 36.3%) and (N = 13,551; 35.8%) respectively.

### 4.2.2 Patients' Demographics

Table 21: Demographics of elderly patients with UTIs over the study period

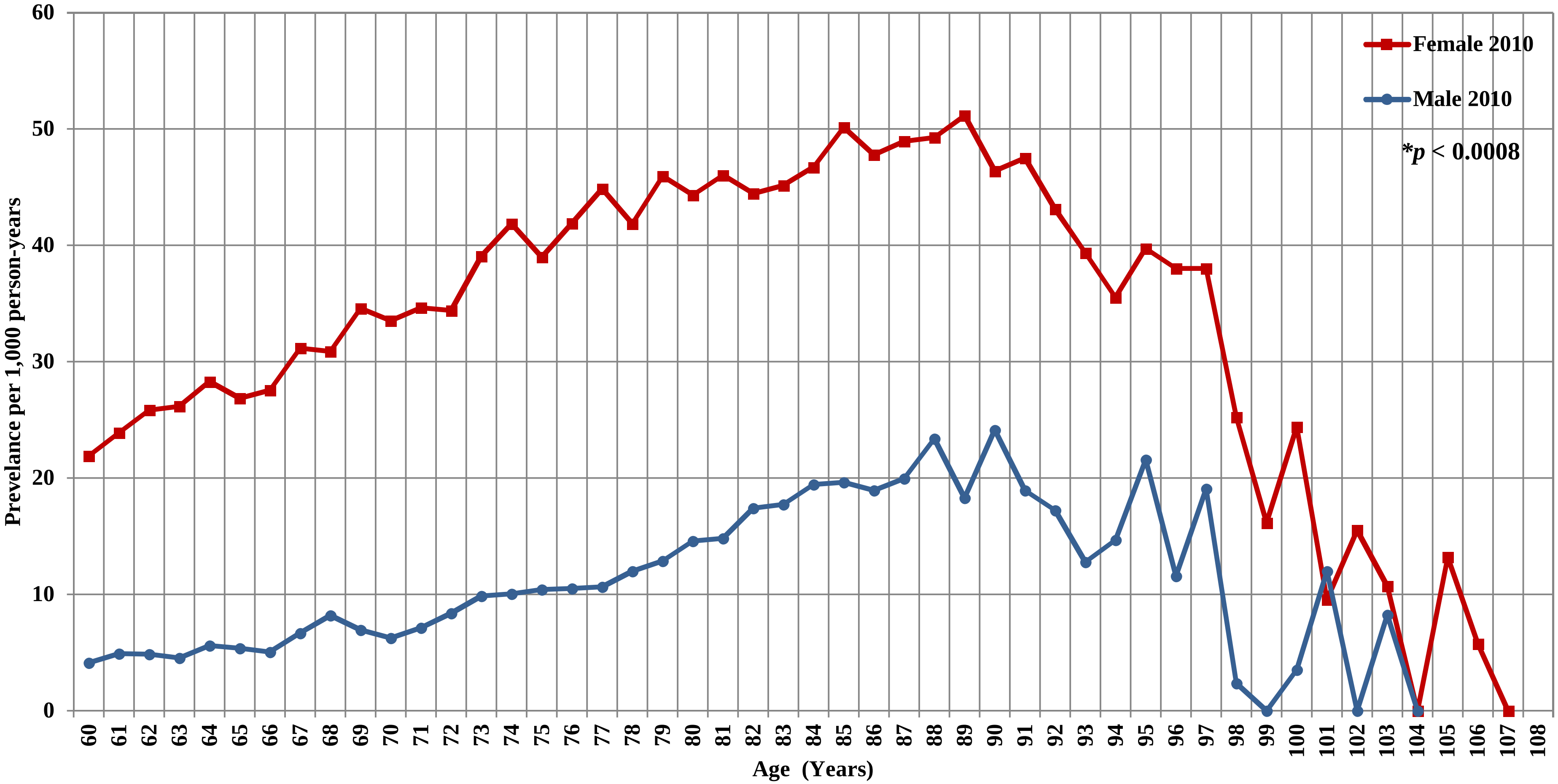
| **Age (mean) ± SD** | 78.81 ± 8.49 | |
|---|---|---|
| **Sex** | **N** | **%** |
| **Female** | 62,913 | 81.4 |
| **Male** | 14,377 | 18.6 |
| **Total** | **77,290** | **100** |

Patients' demographics obtained from the data analysis are shown in Table 21. The mean age of the elderly patients with UTIs from the data extracted from IMS-DA was 78.81 ± 8.49. As the table shows, most of the recorded UTI events were for female patients (N = 62,913; 81.4%) as compared with male patients (N = 14,377; 18.6%).

### 4.2.3 Prevalence of UTIs

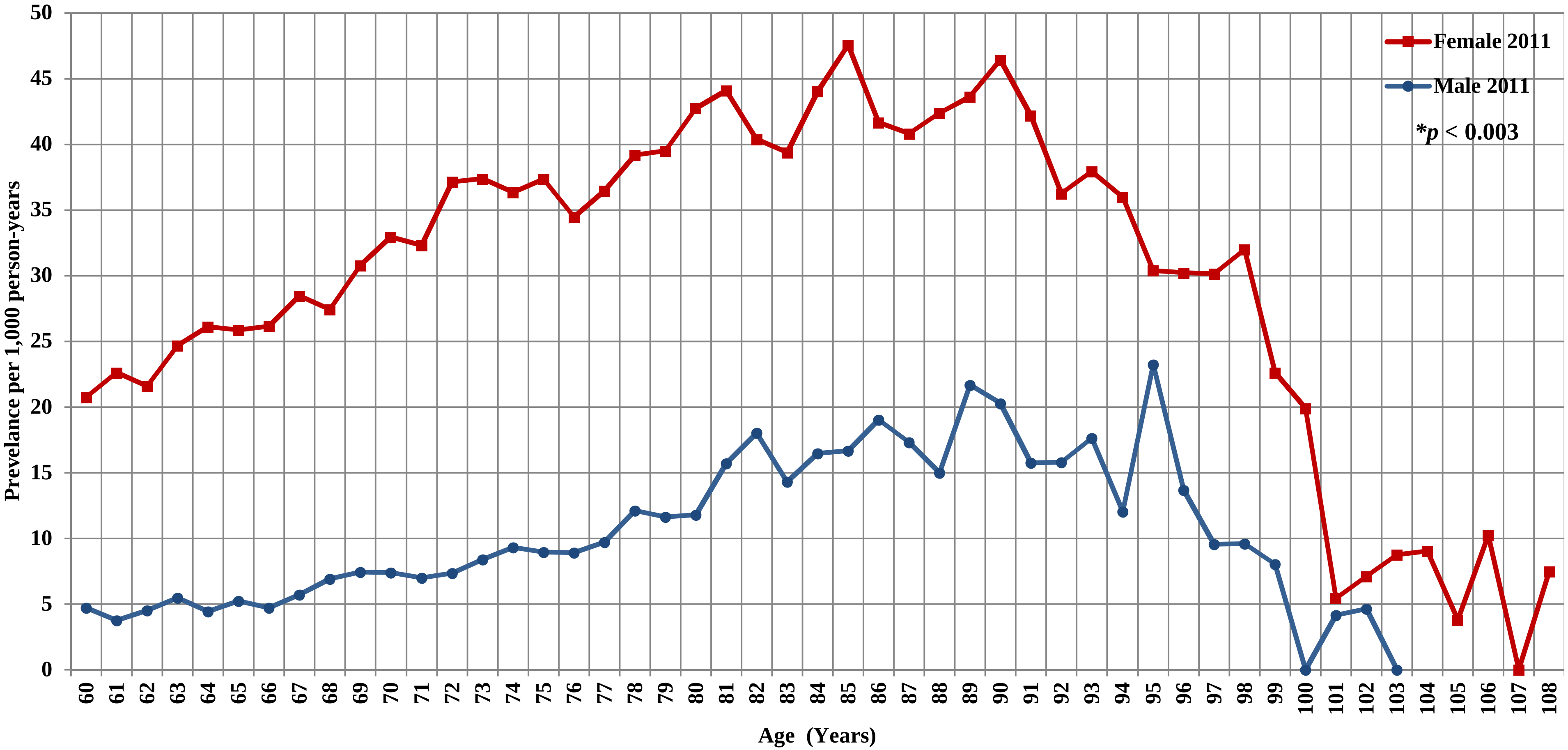
The figures below illustrate the prevalence of UTIs by gender (expressed per 1,000 person-years) for 2010 (Figure 24), 2011 (Figure 25) and 2012 (Figure 26). Results show that prevalence was higher in female in all the three years (statistically significant). Results show that the highest prevalence of UTIs was recorded in 2010 in both genders followed by 2011 then 2012. Throughout the study period, prevalence of UTIs started to increase from the age of 60, reaching its peak in elderly patients of both genders aged 84–93 then starting to decline. The incline in male patients' prevalence over the study period was steady with a gradual increase in its trend, whereas the incline in female patients' prevalence was more progressive. Overall, there was a sharp decline in the prevalence of

UTIs after the age of 93 in both genders. Interestingly, there was a clear fluctuation trend in the prevalence when patients reached the age of 98 especially in female patients.



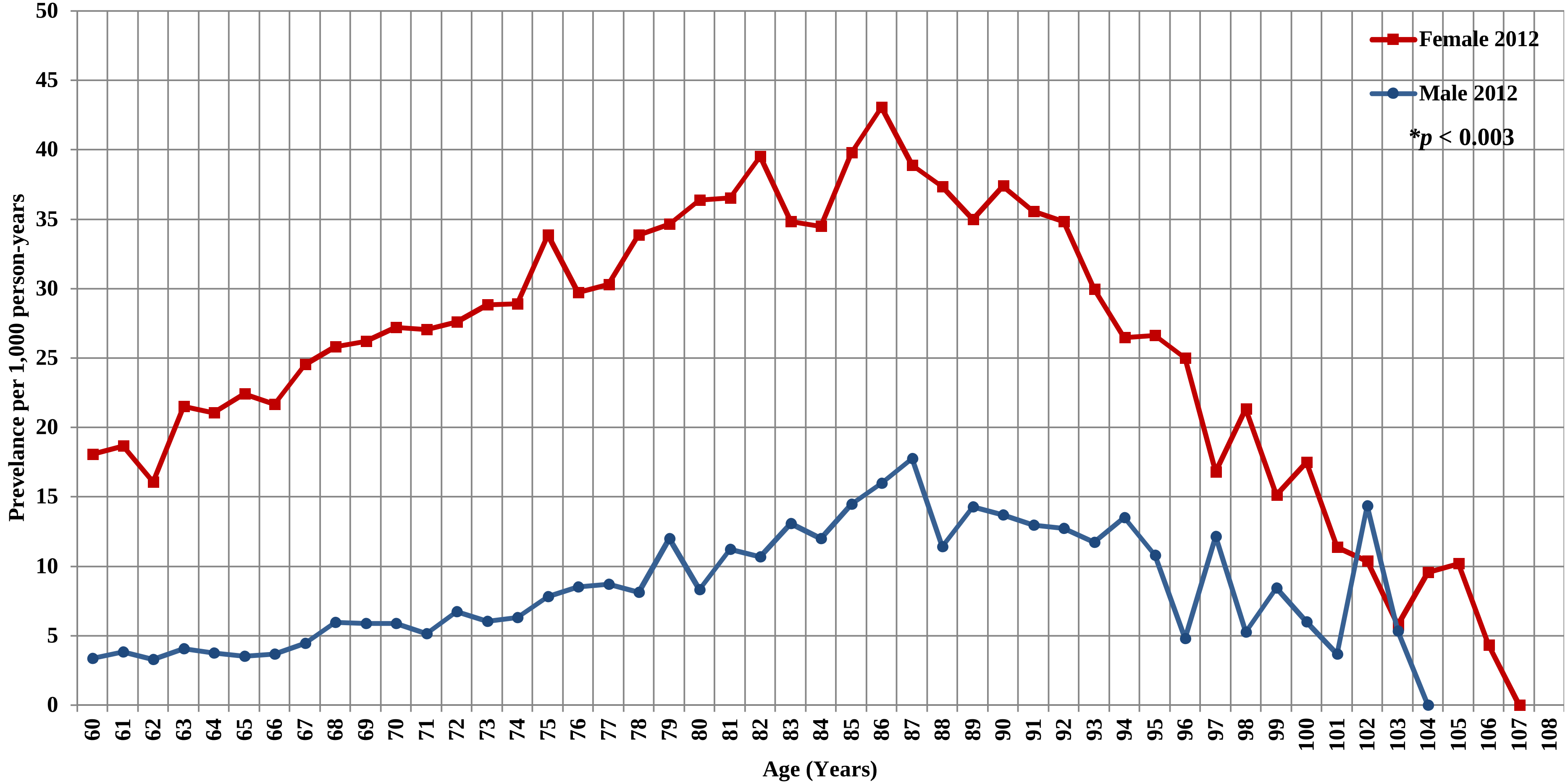

*Student's t–test

Figure 24: Prevalence of UTIs in elderly patients by gender expressed per 1,000 person-years in 2010




*Student's t−test

Figure 25: Prevalence of UTIs in elderly patients by gender expressed per 1,000 person-years in 2011




*Student's t–test

Figure 26: Prevalence of UTIs in elderly patients by gender expressed per 1,000 person-years in 2012

Table 22: Summary of the mean prevalence of UTIs in both male and female elderly patients over the study period

| Gender | Year | Mean prevalence* | 95% C.I. | *p-value* | |
|---|---|---|---|---|---|
| **Females** | 2010 | 34.0 | 30.2-37.8 | $0.71^{¥}$ | $< 0.021^{§}$ |
| | 2011 | 29.8 | 26.2-33.4 | | |
| | 2012 | 26.2 | 23.3-29.1 | | |
| **Males** | 2010 | 11.5 | 9.5-13.5 | $0.92^{¥}$ | |
| | 2011 | 10.8 | 9.1-12.5 | | |
| | 2012 | 8.7 | 7.4-9.9 | | |
| **Age-adjusted** | 2010 | 23.03 | 21.53-24.52 | | |
| | 2011 | 21.10 | 19.67-22.53 | | |
| | 2012 | 17.53 | 16.22-18.83 | | |
| **Age and Sex adjusted** | 2010 | 23.35 | 21.84-24.85 | | |
| | 2011 | 21.44 | 19.99-22.88 | | |
| | 2012 | 17.88 | 16.56-19.19 | | |

*Expressed in 1000 Person-Years; C.I. = Confidence Interval
§ Result was obtained from student's t–test; ¥ Result was obtained from ANOVA test

The mean prevalence of UTIs for both female and male patients during the study period can be found in Table 22. As the table shows, the mean age and sex adjusted UTI prevalence was found to be 23.35 (95% CI 21.84-24.85) per 1,000 person-years for year 2010, 21.44 (95% CI 19.99-22.88) per 1,000 person-years for year 2011 and 17.88 (95% CI 16.56-19.19) per 1,000 person-years. Additionally, there was almost a threefold increase in the mean prevalence of UTIs in female elderly patients compared with male elderly patients. A student's t–test showed a statistically significant result in terms of patients' prevalence with ($p < 0.021$). Overall, there was a decline in the mean prevalence of UTIs in both genders over the study period, which was also noticed in the adjusted age and age–sex mean prevalence.

### 4.2.4 Number of Individual Patient Visits Per Age Group

The number of UTI visits per patient (single individual patient visit(s)) categorised by age group can be seen in Figure 27, in which the number of visits is classified into three main groups. The frequency of visits for each age group was calculated by dividing the number of patients within that specific visit group over the total number of patients within that particular age group for that specific year. Over the study period, the highest number of visits per age group was seen in those aged 85 and older with 6,570 patient visits followed by those aged 75–84 with 6,569 patient visits then those aged 65–74 with 6,568 patient visits. More patients made a single visit to their GP in all age groups over the study period than made multiple visits. The only exception to this was elderly patients aged 85 and older, in which group the highest number of visits was recorded to be three or more (N = 3,450; 52.5%). Detailed numbers on patient visits by year and over the study period can be found in Appendix 18.

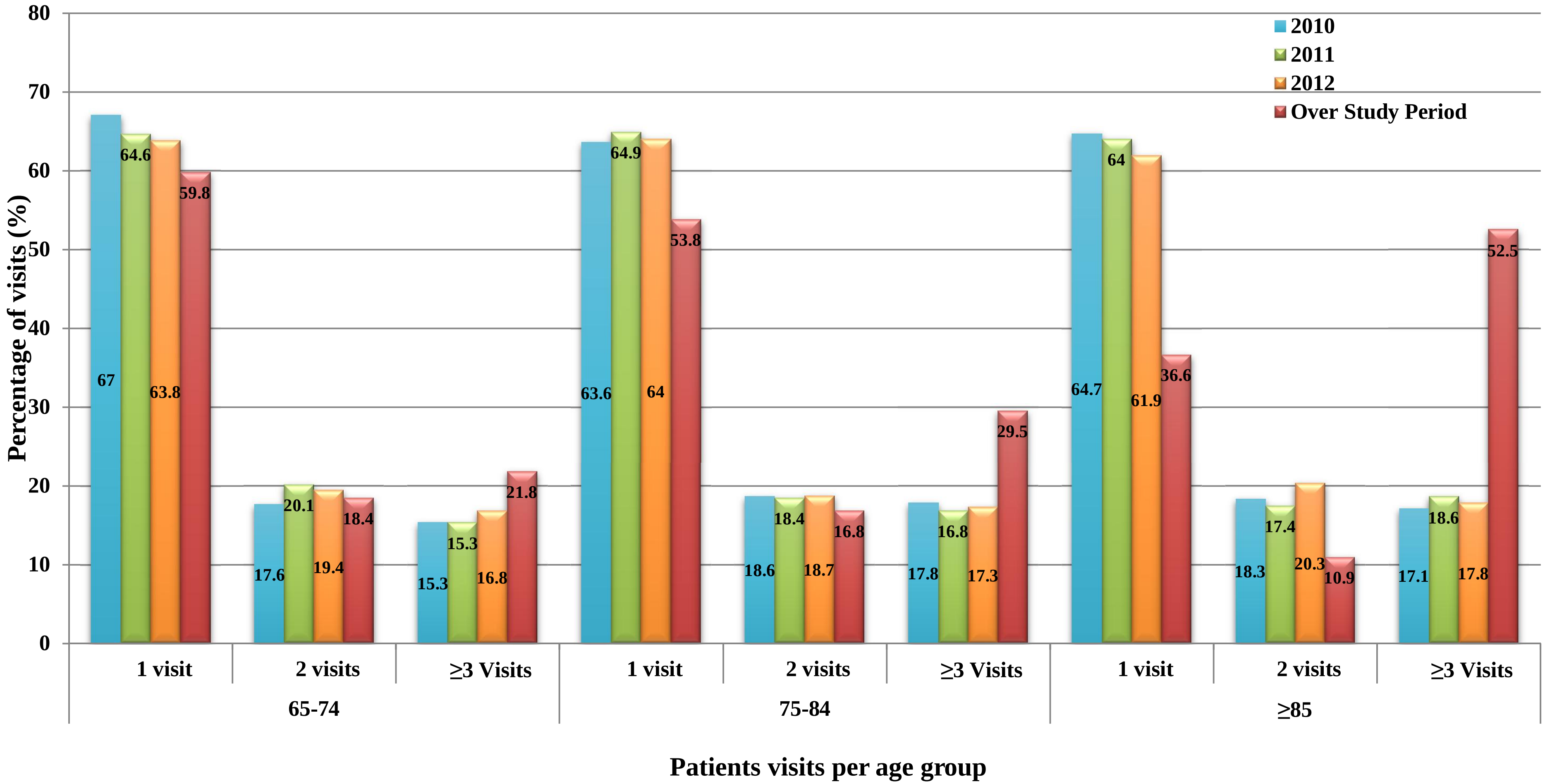



Figure 27: Frequency of individual UTI patients visiting GPs categorised by age group in the 2010–2012 study period

### 4.2.5 Patients' Diagnoses by Gender

The frequency of different types of UTI condition by gender during the study period can be found in Table 23. Unspecified UTI was the most commonly recorded diagnosis by GPs in elderly patients of both genders prescribed antibiotics over the study period. A total of 36,468; (47.18%) patients' visits resulted in at least one antibiotic being prescribed. Unspecified UTI diagnosis was seen in (N =22,463; 72.5%) of female patients compared with (N = 5,084; 92.9%) of male patients, making it the most commonly recorded diagnosis by GPs. Lower UTIs were recorded to be the second most common condition in (N = 8,236; 26.6%) of female patients compared with (N = 332; 6.1%) of male patients. The third most common condition was upper UTI with (N = 215; 0.7%) cases in female patients and (N = 41; 0.7%) in male patients. Other types of UTI were diagnosed in (N = 82; 0.3%) of female patients and (N = 15; 0.3%) of male patients.

Table 23: Frequency of different types of UTI in elderly patients by gender with and without antibiotics therapy over the study period

| Diagnosis | Recorded visits without antibiotics | | | | | | Recorded visits with antibiotics | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Female | | Male | | Total | | Female | | Male | | Total | |
| | **N** | **%** | **N** | **%** | **N** | **%** | **N** | **%** | **N** | **%** | **N** | **%** |
| **UUTIs** | 621 | 0.9 | 226 | 1.57 | 847 | 1.1 | 215 | 0.7 | 41 | 0.7 | 256 | 0.7 |
| **LUTIs** | 15,420 | 24.5 | 940 | 6.54 | 16,360 | 21.2 | 8,236 | 26.6 | 332 | 6.1 | 8,568 | 23.5 |
| **UTI** | 46,623 | 74.1 | 13,122 | 91.27 | 59,745 | 77.3 | 22,463 | 72.5 | 5,084 | 92.9 | 27,547 | 75.5 |
| **Others** | 249 | 0.4 | 89 | 0.62 | 338 | 0.4 | 82 | 0.3 | 15 | 0.3 | 97 | 0.3 |
| **Total** | **62,913** | **100** | **14,377** | **100** | **77,290** | **100** | **30,996** | **100** | **5,472** | **100** | **36,468** | **100** |

UUTIs: Upper UTIs (pyelonephritis); LUTIs: Lower UTIs (Cystitis); UTI: Unspecified UTIs

### 4.2.6 Patients' Diagnoses Categorised by Age Group and Gender

Diagnosis of UTIs according to age group and gender can be found in Table 24, according to which most of the recorded UTIs were seen in those aged 65–74 followed by those aged 75–84 then those aged 85 and older. Unspecified UTI was the highest recorded condition in all patient groups of both genders in all three years with (N = 9,743; 26.7%) in those aged 65–74, (N = 10,044; 27.5%) in those aged 75–84 and (N = 7,760; 21.3%) in those aged 85 and older. In both genders, elderly patients aged 75–84 had more UTIs compared with elderly patients from the other age groups over the three years.

Table 24: Frequency of different types of UTI categorised by age group per year and over the study period for both genders

| **Age (years)** | **Diagnosis** | **2010** | | | | **2011** | | | | **2012** | | | | **2010-2012** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **Female** | | **Male** | | **Female** | | **Male** | | **Female** | | **Male** | | | |
| | | **N** | **%** | **N** | **%** | **N** | **%** | **N** | **%** | **N** | **%** | **N** | **%** | **N** | **%** |
| **65-74** | **UUTIs** | 37 | 0.9 | 4 | 0.6 | 48 | 1.2 | 4 | 0.6 | 27 | 0.7 | 8 | 1.5 | 128 | 0.4 |
| | **LUTIs** | 1,396 | 33.4 | 75 | 11.1 | 1,207 | 29.6 | 36 | 5.0 | 1,195 | 32.8 | 33 | 6.1 | 3,942 | 10.8 |
| | **UTIs** | 2,747 | 65.7 | 598 | 88.3 | 2,807 | 68.9 | 677 | 94.3 | 2,414 | 66.2 | 500 | 92.3 | 9,743 | 26.7 |
| | **Others** | 3 | 0.1 | 0 | 0.0 | 14 | 0.3 | 1 | 0.1 | 9 | 0.2 | 1 | 0.2 | 28 | 0.1 |
| **Total** | | **4,183** | **100** | **677** | **100** | **4,076** | **100** | **718** | **100** | **3,645** | **100** | **542** | **100** | **13,841** | **38.0** |
| **75-84** | **UUTIs** | 23 | 0.5 | 7 | 0.9 | 30 | 0.8 | 2 | 0.3 | 36 | 1.1 | 12 | 2.0 | 110 | 0.3 |
| | **LUTIs** | 1,202 | 28 | 51 | 6.7 | 1,008 | 27.0 | 29 | 4.1 | 936 | 27.7 | 48 | 8.0 | 3,274 | 9.0 |
| | **UTIs** | 3,049 | 70.9 | 697 | 91.6 | 2,673 | 71.7 | 680 | 95.2 | 2,406 | 71.1 | 539 | 89.7 | 10,044 | 27.5 |
| | **Others** | 25 | 0.6 | 6 | 0.8 | 19 | 0.5 | 3 | 0.4 | 7 | 0.2 | 2 | 0.3 | 62 | 0.2 |
| **Total** | | **4,299** | **100** | **761** | **100** | **3,730** | **100** | **714** | **100** | **3,385** | **100** | **601** | **100** | **13,490** | **37** |
| **≥85** | **UUTIs** | 4 | 0.1 | 3 | 0.6 | 4 | 0.2 | 0 | 0.0 | 6 | 0.3 | 1 | 0.2 | 18 | 0.0 |
| | **LUTIs** | 454 | 17.0 | 28 | 5.5 | 425 | 16.1 | 13 | 2.6 | 413 | 17.4 | 19 | 4.3 | 1,352 | 3.7 |
| | **UTIs** | 2,211 | 82.8 | 478 | 93.7 | 2,207 | 83.7 | 490 | 97.2 | 1,949 | 82.3 | 425 | 95.5 | 7,760 | 21.3 |
| | **Others** | 2 | 0.1 | 1 | 0.2 | 2 | 0.1 | 1 | 0.2 | 1 | 0 | 0 | 0 | 7 | 0 |
| **Total** | | **2,671** | **100** | **510** | **100** | **2,638** | **100** | **504** | **100** | **2,369** | **100** | **445** | **100** | **9,137** | **100** |

UUTIs: Upper UTIs (pyelonephritis); LUTIs: Lower UTIs (Cystitis); UTI: Unspecified UTIs

### 4.2.7 Antibiotics Prescribing

For elderly patients, the number of antibiotics prescribed for UTIs compared with the total number of antibiotics prescribed during the study period is presented in Table 25.

Table 25: Frequency of antibiotics prescribing for UTIs compared with the number of total antibiotics prescriptions for elderly patients

| Year | Total elderly antibiotics prescriptions | UTIs antibiotics prescriptions | Of total UTIs antibiotics prescription | Of total elderly antibiotic prescriptions |
|---|---|---|---|---|
| | N | N | % | % |
| **2010** | 52,263 | 13,551 | 35.8 | 25.9 |
| **2011** | 53,589 | 12,849 | 34.0 | 23.9 |
| **2012** | 49,266 | 11,415 | 30.2 | 23.2 |
| **Total** | **155,118** | **37,815** | **100** | **24.4** |

The number of antibiotics prescribed for UTIs was 37,815 resulting from 36,468 visits by 1,083 patients who received at least one antibiotic. The highest number of antibiotics prescribed for UTIs was in 2010 with (13,551; 25.9%) prescriptions followed by 2011 with (12,849; 23.9%) prescriptions then 2012 with (11,415; 23.2%) prescriptions. Antibiotic prescriptions for the treatment of UTIs accounted for (N = 37,815; 24.4%) of the total antibiotics prescriptions for elderly patients within the study period with the highest prescribing seen in 2012 (11,415; 23.2%). As the table shows, there was a declining trend in the frequency of prescribing antibiotics for UTIs over the years.

Table 26: Frequency of antibiotics prescriptions for UTIs by age and year over the study period

| Age group (years) | 2010 | | 2011 | | 2012 | | 2010-2012 | |
|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % |
| **65-74** | 5,013 | 37.0 | 4,973 | 38.7 | 4,348 | 38.1 | 14,334 | 37.9 |
| **75-84** | 5,235 | 38.6 | 4,616 | 35.9 | 4,137 | 36.2 | 13,988 | 37.0 |
| **≥85** | 3,303 | 24.4 | 3,260 | 25.4 | 2,930 | 25.7 | 9,493 | 25.1 |
| **Total** | **13,551** | **100** | **12,849** | **100** | **11,415** | **100** | **37,815** | **100** |

Table 26 shows the frequency of antibiotic prescriptions for UTIs according to patient age group. Over the study period, the general trend of antibiotics prescribing can be seen to decline with advancing age. Patients aged 65–74 had the highest frequency of antibiotics prescriptions for UTIs with (N = 14,334; 37.9%) prescriptions, followed by those aged 75–84 (N = 13,988; 37%) and those aged 85 and older (N = 9,493; 25.1%). In 2010, the number of issued prescriptions was highest in the 75–84 age group (N = 5,235; 38.6%), whereas in 2011 and 2012 the highest number of issued prescriptions was in the

65–74 age group with (N = 4,973; 38.7%) and (N = 4,348; 38.1) prescriptions respectively.

Figure 28 shows the antibiotics most frequently prescribed by GPs for UTIs in elderly patients. Throughout the study period, trimethoprim, nitrofurantoin, cephalexin, co-amoxiclav, ciprofloxacin and amoxicillin were the most commonly prescribed antibiotics with (N = 15,772; 41.7%), (N = 9,448; 25%), (N = 5,042; 13.3%), (N = 2350; 6.2%), (N = 1,920; 5.1%) and (N = 1,866; 4.9%) respectively. What is interesting in this figure is that nitrofurantoin prescribing was increasing on a yearly basis with the highest prescribing seen in 2012. However, this increase was not significant as shown by the result from Chi−square ($p < 0.11$), whereas the prescribing of trimethoprim, cephalexin and ciprofloxacin was declining over the years. There was a slight decline in co-amoxiclav prescribing in 2011 followed by a slight incline in its prescribing in 2012. Amoxicillin was prescribed at a steady rate over the years. Prescribing of other antibiotics[28] decreased over the years to reach its lowest level in 2012. Detailed numbers of antibiotics prescribed by GPs by year and over the study period can be seen in Appendix 19.

[28] Any antibiotic that was prescribed for UTIs other those listed in the figure.

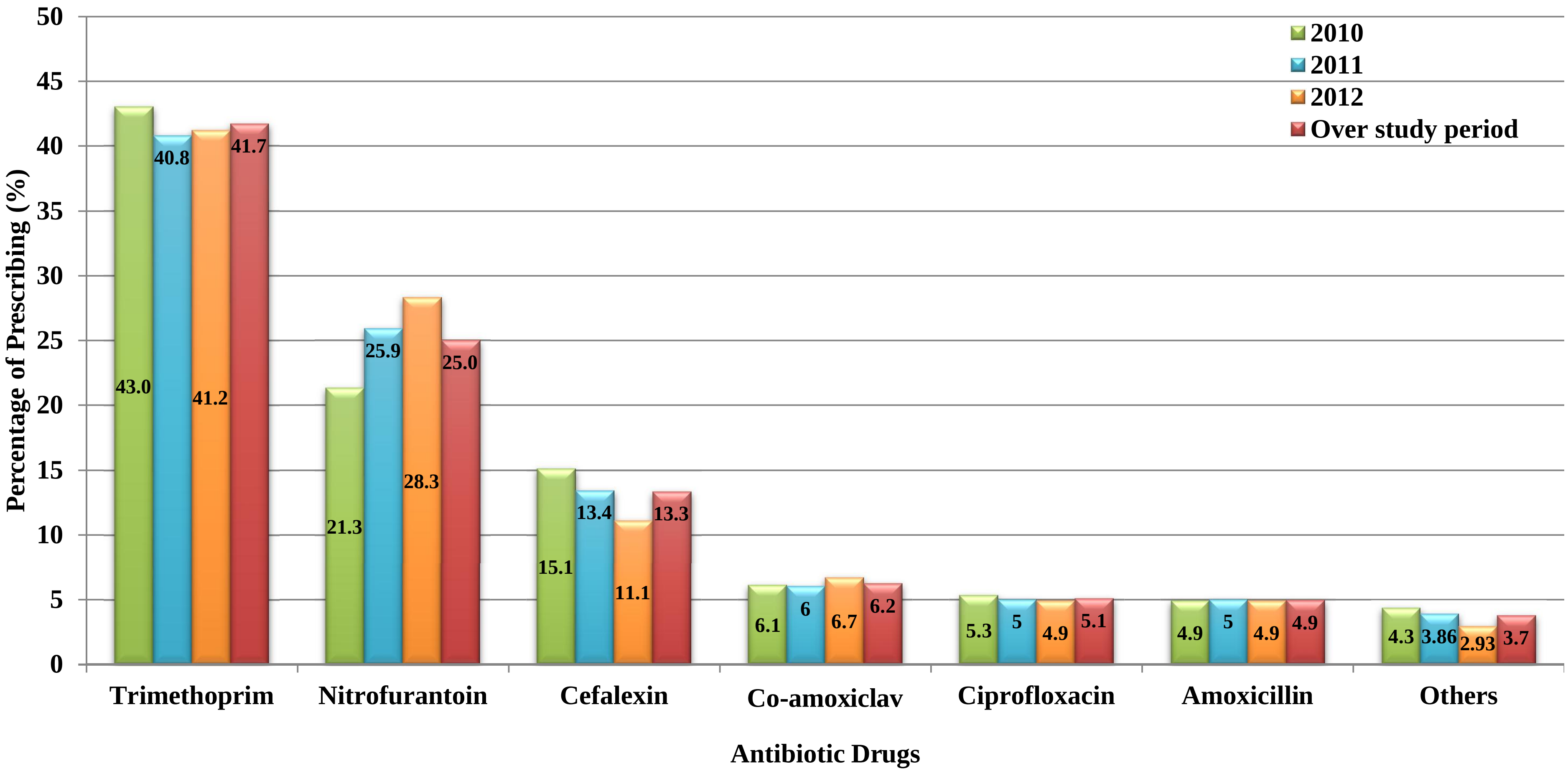



Figure 28: Prescribing trends for the most frequently prescribed antibiotics for UTIs in elderly patients presented by year

Table 27: Frequency of commonly prescribed antibiotics classified according to UTI type

| Antibiotic | UUTIs | | LUTIs | | UTIs | | Others | |
|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % |
| Trimethoprim | 67 | 24.9 | 4,311 | 49.0 | 11,361 | 39.6 | 33 | 33.7 |
| Nitrofurantoin | 45 | 16.7 | 2,238 | 25.4 | 7,140 | 24.9 | 25 | 25.5 |
| Cefalexin | 31 | 11.5 | 987 | 11.2 | 4,006 | 14.0 | 18 | 18.4 |
| Co-amoxiclav | 48 | 17.8 | 374 | 4.3 | 1,917 | 6.7 | 11 | 11.2 |
| Ciprofloxacin | 47 | 17.5 | 285 | 3.2 | 1,583 | 5.5 | 5 | 5.1 |
| Amoxicillin | 20 | 7.4 | 332 | 3.8 | 1,513 | 5.3 | 1 | 1.0 |

UUTIs: Upper UTIs (pyelonephritis); LUTIs: Lower UTIs (Cystitis); UTI: Unspecified UTIs

The most commonly prescribed antibiotics according to UTI diagnosis can be found in Table 27. Of the patients with an unspecified UTI diagnosis, (N = 11,361; 39.6%) received trimethoprim, (N = 7,140; 24.9%) received nitrofurantoin and (N = 4,006; 14%) were prescribed cephalexin. Of those with upper UTIs, (N = 67; 24.9%) received trimethoprim, (N = 48; 17.8%) were prescribed co-amoxiclav and (N = 47; 17.5%) received ciprofloxacin. Of the patients with lower UTIs, (N = 4,311; 49%) received trimethoprim, (N = 2,238; 25.4%) were prescribed nitrofurantoin and (N = 987; 11.2%) were prescribed cephalexin.

### 4.2.8 Prescribed Antibiotics Durations

The duration of antibiotics treatment prescribed by GPs for different types of UTI in different age groups can be found in Table 28. In patients aged 65–74, frequency table shows that the most commonly prescribed antibiotics and their durations were trimethoprim for seven days (N = 2,310; 38.4%) followed by nitrofurantoin for more than 28 days (N = 1,752; 46.3%), cephalexin for seven days (1,204; 66%), co-amoxiclav mostly for seven days (N = 662; 80.2%), ciprofloxacin for more than 28 days (N = 351; 50.2%) and amoxicillin for seven days (N = 338; 54.1%).

In patients aged 75–84, the most frequently prescribed antibiotics and their durations were trimethoprim for seven days (N = 2,483; 42.2%) followed by nitrofurantoin for more than 28 days (N = 1,551; 45.5%), cephalexin for seven days (N = 1,206; 63.6%), co-amoxiclav for seven days (N = 597; 70.4%), ciprofloxacin for more than 28 days (N = 384; 56.2%) and amoxicillin for seven days (N = 396; 55%).

In patients aged 85 and older, the most commonly prescribed antibiotics and their durations were trimethoprim for seven days (N = 1,711; 44.2%), nitrofurantoin for more than 28 days (N = 1,063; 47.3%), cephalexin for seven days (N = 797; 60.2%), co-amoxiclav for seven days (N = 473; 69.9%), ciprofloxacin for more than 28 days (N = 334; 62.1%) and amoxicillin for more than 28 days (N = 250; 48%).

Table 28: Frequency of antibiotics for UTIs categorised by age group and duration of therapy

| Age (years) | Antibiotic | 3 Days | | 7 Days | | 10-14 Days | | 28 Days | | Others | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | % | N | % | N | % | N | % | N | % |
| 65-74 | Trimethoprim | 2,107 | 35.0 | 2,310 | 38.4 | 102 | 1.7 | 172 | 2.9 | 1,325 | 22.0 |
| | Nitrofurantoin | 283 | 7.5 | 1,577 | 41.6 | 98 | 2.6 | 77 | 2.0 | 1,752 | 46.3 |
| | Cefalexin | 60 | 3.3 | 1204 | 66.0 | 71 | 3.9 | 94 | 5.2 | 394 | 21.6 |
| | Co-amoxiclav | 18 | 2.2 | 662 | 80.2 | 48 | 5.8 | 4 | 0.5 | 93 | 11.3 |
| | Ciprofloxacin | 7 | 1.0 | 171 | 24.5 | 153 | 21.9 | 17 | 2.4 | 351 | 50.2 |
| | Amoxicillin | 23 | 3.7 | 338 | 54.1 | 27 | 4.3 | 3 | 0.5 | 234 | 37.4 |
| 75-84 | Trimethoprim | 1,709 | 29.0 | 2,483 | 42.2 | 102 | 1.7 | 212 | 3.6 | 1,378 | 23.4 |
| | Nitrofurantoin | 245 | 7.2 | 1,479 | 43.3 | 70 | 2.1 | 67 | 2.0 | 1,551 | 45.5 |
| | Cefalexin | 60 | 3.2 | 1,206 | 63.6 | 56 | 3.0 | 107 | 5.6 | 467 | 24.6 |
| | Co-amoxiclav | 24 | 2.8 | 597 | 70.4 | 36 | 4.2 | 14 | 1.7 | 177 | 20.9 |
| | Ciprofloxacin | 26 | 3.8 | 167 | 24.5 | 99 | 14.5 | 7 | 1.0 | 384 | 56.2 |
| | Amoxicillin | 20 | 2.8 | 396 | 55.0 | 21 | 2.9 | 4 | 0.6 | 279 | 38.8 |
| ≥85 | Trimethoprim | 930 | 24.0 | 1,711 | 44.2 | 54 | 1.4 | 142 | 3.7 | 1,035 | 26.7 |
| | Nitrofurantoin | 148 | 6.6 | 946 | 42.1 | 34 | 1.5 | 58 | 2.6 | 1,063 | 47.3 |
| | Cefalexin | 45 | 3.4 | 797 | 60.2 | 48 | 3.6 | 57 | 4.3 | 376 | 28.4 |
| | Co-amoxiclav | 28 | 4.1 | 473 | 69.9 | 35 | 5.2 | 8 | 1.2 | 133 | 19.6 |
| | Ciprofloxacin | 19 | 3.5 | 110 | 20.4 | 72 | 13.4 | 3 | 0.6 | 334 | 62.1 |
| | Amoxicillin | 12 | 2.3 | 250 | 48.0 | 14 | 2.7 | 8 | 1.5 | 237 | 45.5 |

### 4.2.9 GPs' Adherence to UTI Good Practice Points

To evaluate GPs' adherence to good practice points, tables were generated to compare the antibiotics prescribed for UTIs in elderly patients against the SAPG good practice points for female patients (Table 29) and for male patients (Table 30). The results show that trimethoprim was prescribed in line with the good practice points in (N = 1,617; 38.9%) of female patients and (N = 85; 54.1%) of male patients with LUTIs, and nitrofurantoin was prescribed appropriately in (N = 190; 8.9%) of female patients and (N = 49; 50%) of male patients with LUTIs. Use of broad-spectrum antibiotics should be avoided in elderly patients to avoid *Clostridium difficile* infection. However, the results showed that (N = 9,125; 24.1%) broad-spectrum antibiotics prescriptions were issued for both genders, including for ciprofloxacin (N = 1,733; 4.6%)[29], co-amoxiclav (N = 2,350; 6.2%) and cephalexin (N = 5,042; 13.3%). Moreover, (N = 12,159; 32.2%) of antibiotics prescriptions were prescribed for durations other than the recommended either for treatment or for prophylaxis; this was seen in (N = 10,605; 33%) of female patients' total UTI antibiotics prescriptions and in (N = 1,554; 27.5%) of male patients' total UTI antibiotics prescriptions.

[29] Prescriptions for male prostatitis were excluded from this number.

Table 29: Antibiotics prescribing for UTIs in female patients categorised according to condition and duration over the study period

| Antibiotic | Duration | UUTIs | | LUTIs | | UTIs | | Others | |
|---|---|---|---|---|---|---|---|---|---|
| | | N | % | N | % | N | % | N | % |
| **Trimethoprim** | 3 days | 13 | 22.4 | 1,617 | 38.9 | 2,923 | 31.3 | 6 | 24 |
| | 7 days | 39 | 67.2 | 1,367 | 32.9 | 3,710 | 39.7 | 8 | 32 |
| | 10-14 days | 2 | 3.4 | 44 | 1.1 | 120 | 1.3 | 2 | 8 |
| | 28 days | 1 | 1.7 | 74 | 1.8 | 359 | 3.8 | 0 | 0 |
| | Other[30] | 3 | 5.2 | 1,052 | 25.3 | 2,227 | 23.8 | 9 | 36 |
| **Nitrofurantoin** | 3 days | 3 | 7.5 | 190 | 8.9 | 463 | 7.6 | 0 | 0 |
| | 7 days | 19 | 47.5 | 901 | 42.1 | 2,475 | 40.8 | 11 | 45.8 |
| | 10-14 days | 0 | 0 | 36 | 1.7 | 123 | 2 | 3 | 12.5 |
| | 28 days | 0 | 0 | 28 | 1.3 | 151 | 2.5 | 1 | 4.2 |
| | Other | 18 | 45.0 | 985 | 46 | 2,855 | 47.1 | 9 | 37.5 |
| **Cefalexin** | 3 days | 0 | 0 | 34 | 3.5 | 127 | 3.7 | 1 | 6.3 |
| | 7 days | 21 | 75.0 | 614 | 64 | 2,091 | 61.2 | 11 | 68.8 |
| | 10-14 days | 0 | 0 | 20 | 2.1 | 131 | 3.8 | 0 | 0 |
| | 28 days | 3 | 10.7 | 57 | 5.9 | 177 | 5.2 | 0 | 0 |
| | Other | 4 | 14.3 | 235 | 24.5 | 889 | 26.0 | 4 | 25 |
| **Co-amoxiclav** | 3 days | 0 | 0 | 11 | 3.1 | 57 | 4.1 | 0 | 0 |
| | 7 days | 33 | 89.2 | 263 | 73.7 | 1,015 | 72.3 | 4 | 44.4 |
| | 10-14 days | 3 | 8.1 | 14 | 3.9 | 65 | 4.6 | 1 | 11.1 |
| | 28 days | 0 | 0 | 3 | 0.8 | 18 | 1.3 | 0 | 0 |
| | Other | 1 | 2.7 | 66 | 18.5 | 248 | 17.7 | 4 | 44.4 |
| **Ciprofloxacin** | 3 days | 1 | 2.7 | 11 | 4.1 | 35 | 3.2 | 0 | 0 |
| | 7 days | 15 | 40.5 | 56 | 20.9 | 244 | 22 | 1 | 25 |
| | 10-14 days | 10 | 27.0 | 25 | 9.3 | 161 | 14.5 | 0 | 0 |
| | 28 days | 0 | 0 | 5 | 1.9 | 7 | 0.6 | 0 | 0 |
| | Other | 11 | 29.7 | 171 | 63.8 | 661 | 59.7 | 3 | 75 |
| **Amoxicillin** | 3 days | 0 | 0 | 12 | 3.7 | 41 | 3.5 | 0 | 0 |
| | 7 days | 11 | 57.9 | 177 | 55 | 576 | 49.1 | 0 | 0 |
| | 10-14 days | 3 | 15.8 | 6 | 1.9 | 38 | 3.2 | 0 | 0 |
| | 28 days | 0 | 0 | 1 | 0.3 | 7 | 0.6 | 0 | 0 |
| | Other | 5 | 26.3 | 126 | 39.1 | 511 | 43.6 | 0 | 0 |

UUTIs: Upper UTIs (pyelonephritis); LUTIs: Lower UTIs (Cystitis); UTI: Unspecified UTIs

[30] Referred to treatment duration other than the recommended.

Table 30: Antibiotics prescribing for UTIs in male patients categorised according to condition and duration over the study period

| Antibiotic | Duration | UUTIs | | LUTIs | | UTIs | | Others | |
|---|---|---|---|---|---|---|---|---|---|
| | | N | % | N | % | N | % | N | % |
| **Trimethoprim** | 3 days | 0 | 0 | 19 | 12.1 | 168 | 8.3 | 0 | 0 |
| | 7 days | 5 | 55.6 | 85 | 54.1 | 1,285 | 63.6 | 5 | 62.5 |
| | 10-14 days | 0 | 0 | 5 | 3.2 | 85 | 4.2 | 0 | 0 |
| | 28 days | 0 | 0 | 2 | 1.3 | 87 | 4.3 | 3 | 37.5 |
| | Other | 4 | 44.4 | 46 | 29.3 | 397 | 19.6 | 0 | 0 |
| **Nitrofurantoin** | 3 days | 0 | 0 | 3 | 3.1 | 17 | 1.6 | 0 | 0 |
| | 7 days | 1 | 20 | 49 | 50 | 546 | 50.9 | 0 | 0 |
| | 10-14 days | 0 | 0 | 6 | 6.1 | 34 | 3.2 | 0 | 0 |
| | 28 days | 0 | 0 | 3 | 3.1 | 19 | 1.8 | 0 | 0 |
| | Other | 4 | 80 | 37 | 37.8 | 457 | 42.6 | 1 | 100 |
| **Cefalexin** | 3 days | 0 | 0 | 0 | 0 | 3 | 0.5 | 0 | 0 |
| | 7 days | 3 | 100 | 22 | 81.5 | 443 | 75 | 2 | 100 |
| | 10-14 days | 0 | 0 | 1 | 3.7 | 23 | 3.9 | 0 | 0 |
| | 28 days | 0 | 0 | 1 | 3.7 | 20 | 3.4 | 0 | 0 |
| | Other | 0 | 0 | 3 | 11.1 | 102 | 17.3 | 0 | 0 |
| **Co-amoxiclav** | 3 days | 0 | 0 | 0 | 0 | 2 | 0.4 | 0 | 0 |
| | 7 days | 10 | 90.9 | 12 | 70.6 | 393 | 76.5 | 2 | 100 |
| | 10-14 days | 1 | 9.1 | 0 | 0 | 35 | 6.8 | 0 | 0 |
| | 28 days | 0 | 0 | 1 | 5.9 | 4 | 0.8 | 0 | 0 |
| | Other | 0 | 0 | 4 | 23.5 | 80 | 15.6 | 0 | 0 |
| **Ciprofloxacin** | 3 days | 0 | 0 | 0 | 0.0 | 5 | 1.1 | 0 | 0 |
| | 7 days | 4 | 40 | 4 | 23.5 | 124 | 26.1 | 0 | 0 |
| | 10-14 days | 3 | 30 | 5 | 29.4 | 120 | 25.3 | 0 | 0 |
| | 28 days | 0 | 0 | 19 | 12.1 | 168 | 8.3 | 0 | 0 |
| | Other | 5 | 55.6 | 85 | 54.1 | 1285 | 63.6 | 5 | 62.5 |
| **Amoxicillin** | 3 days | 0 | 0 | 5 | 3.2 | 85 | 4.2 | 0 | 0 |
| | 7 days | 0 | 0 | 2 | 1.3 | 87 | 4.3 | 3 | 37.5 |
| | 10-14 days | 4 | 44.4 | 46 | 29.3 | 397 | 19.6 | 0 | 0 |
| | 28 days | 0 | 0 | 3 | 3.1 | 17 | 1.6 | 0 | 0 |
| | Other | 1 | 20 | 49 | 50 | 546 | 50.9 | 0 | 0 |

UUTIs: Upper UTIs (pyelonephritis); LUTIs: Lower UTIs (Cystitis); UTI: Unspecified UTIs

## 4.3 Discussion

This section of the chapter discusses and interprets the research results and compares them with the results from the relevant reviewed literature in Chapter Two. The application of a quantitative DUR research was successful in describing the prevalence of UTIs in elderly people in addition to auditing GPs' antibiotics prescribing for UTIs in the UK. The study showed that UTIs were significantly ($p < 0.021$) far more prevalent in female patients compared with male patients in the study period 2010–2012 as well as overall within the patient age groups 65–74, 75–84 and 85 and older (Figure 24), (Figure 25) and (Figure 26). Unspecified UTIs were found to be the most commonly recorded conditions throughout the study period in 75.5% (N = 22,547) of all recorded events followed by lower UTIs in 23.5% (N = 8,568) of recorded events in elderly patients. Perhaps a good explanation for this high prevalence in females is the presence of certain gender-related factors such as the anatomical structure of the female urethra, increased incidence of urinary incontinence, previous and recurrent history of UTIs, presence of DM, low oestrogen level as well as longer life expectancy in females compared with males (Moore and Spence 2014). The findings from the DUR study were consistent with the findings of several other epidemiological studies (Ruben *et al.* 1995, Ki *et al.* 2004, Czaja *et al.* 2007, Laupland *et al.* 2007, Caljouw *et al.* 2011), all of which agreed that UTIs were significantly higher in females compared with males, except Omoregie *et al.* (2010), who found the prevalence of UTIs to be higher in males aged 60 and over compared with females. Overall, the prevalence of UTIs in the UK was found to be declining over the study years. The highest prevalence was seen in 2010 followed by 2011 then 2012. There were several possible explanations for this decline in prevalence, for example, the increase in the death rate among the elderly patients who were registered with the surgeries from which the study data were obtained. In this study, the mean age for elderly patients with UTIs was found to be 78.81 ± 8.49. In the UK, the reported life expectancy for males aged 85 was 5.8 years (90.8) whereas for females it was 6.8 years (91.8) for the period 2010–2012 (ONS 2014). Data from the ONS showed that in just one year there were 5.4% more deaths equating to almost 27,000 extra deaths (ONS 2016). Figures from the report showed that numbers of deaths have fallen steadily since the 1970s, but that trend began to reverse in 2011 (ONS 2014). This could explain why females tend to have UTIs at an older age than males. Another possible explanation for this reduction over the study period is the increase in the total number of elderly population in the UK (ONS 2015a), which in turn reflects the total number of elderly patients who visited GP surgeries. A final explanation might be that some elderly patients moved from one catchment area to another and thus were following up with a different GP.

From an age perspective, the majority of recorded visits to GP surgeries for UTIs were found to be highest among elderly patients aged 84–93. Although the number of elderly patients within this category was lowest compared with the other two age categories (65–74 and 75–84), frequent GP visits by this age group might explain the high prevalence and peaks shown in Figures 24, 25 and 26 in Chapter Four. This is in line with both Laupland *et al.* (2007) who found elderly people who were 90 or older had the highest UTI incidence among all age groups with 925.7 for females, 637.8 for males and 850.6 overall per 1,000 per year and Eriksson *et al.* (2010) who found the prevalence to be 25% for patients aged 85, 29.6% for patients aged 90 and 34.4% for those aged 95 and over. Perhaps this increase in the number of visits was a result of age-associated changes in immunity (Beveridge *et al.* 2011), cognitive impairment, urinary incontinence and prior or recent history of UTI (Hu *et al.* 2004, Foxman 2014) or other risk factors for UTI as shown in Table 10 in Chapter One. The prevalence of UTIs was noticed to started to increase from the age of 60, reaching its peak between 84 and 93 before declining from the age of 93, in both genders. In this DUR study, the age trend of elderly patients with UTIs was similar to the findings described by Laupland *et al.* (2007), who found the estimated incidence in females to be 40 for those aged 60–69, 46 for those aged 70–79 and 110 for those aged 80–89, all expressed in 1,000 per year, and in males to be 10 for those aged 60–69, 15 for those aged 70–79 and 60 for those aged 80–89, all expressed in 1,000 per year; and partially to those reported by Ki *et al.* (2004), who described similar findings in elderly female patients with incidence of 57.15 per 10,000 population for the 60–79 age group and 28.07 per 10,000 population for the 80 and over age group, but not in elderly male patients. Additionally, this result was found to be partly in agreement with the results of other epidemiological studies (Ruben *et al.* 1995, Malmsten *et al.* 1997, Molander *et al.* 2000, Galatti *et al.* 2006, Czaja *et al.* 2007, Eriksson *et al.* 2010, Marques *et al.* 2012), who either linked the increased UTI incidence or prevalence with advancing age compared with other age groups in general and in elderly patients with this age in particular or they did not describe the trend in detail beyond the age of 90 (Ruben *et al.* 1995, Molander *et al.* 2000, Foxman *et al.* 2000, Ki *et al.* 2004, Galatti *et al.* 2006, Czaja *et al.* 2007, Laupland *et al.* 2007, Caljouw *et al.* 2011, Marques *et al.* 2012). On the other hand, the results of this DUR study did not support Foxman *et al.* (2000), who found that

UTIs do not increase with age in the female gender, or Omoregie *et al.* (2010), who stated that UTI prevalence decreases with age. Perhaps the discrepancies in the reported epidemiology among different studies are owing to the heterogeneity in the study sample sizes caused by including smaller numbers of elderly patients compared with other age groups, to differences in recruitment settings or to differences in study methodology. Some of these studies included a small sample size of elderly patients with UTIs while other studies included other age groups (Malmsten et al. 1997, Foxman *et al.* 2000, Ki *et al*. 2004, Galatti *et al.* 2006, Czaja *et al.* 2007, Laupland *et al.* 2007). Although some studies focused only on the elderly population (Ruben *et al.* 1995, Molander *et al.* 2000, Eriksson *et al.* 2010, Omoregie *et al.* 2010, Caljouw *et al.* 2011, Marques *et al.* 2012), instead of recruiting patients from a non-institutionalised, community setting, they recruited patients from different settings such as hospitals and nursing homes (Malmsten *et al.* 1997, Molander *et al.* 2000, Laupland *et al.* 2007, Eriksson *et al.* 2010, Omoregie *et al.* 2010, Marques *et al.* 2012). One possible explanation for these discrepancies is the shift in some countries' population structure towards an ageing population compared with other countries over the years as reported by Hestbaek *et al.*(2014), which resulted primarily from improvements in healthcare services provided to this age group (Hestbaek *et al.* 2014). Another possible reason for these discrepancies may be related to the differentiation between UTIs and ASB, which can be easily distinguished in studies that based their results on laboratory findings and clinical presentation (Laupland *et al.* 2007, Caljouw *et al.* 2011, Marques *et al.* 2012) but are less easy to separate in studies that depend solely on either survey (Ruben *et al.* 1995, Malmsten *et al.* 1997, Foxman *et al.* 2000, Molander *et al.* 2000) or computerised database (Ki *et al.* 2004, Galatti *et al.* 2006, Czaja *et al.* 2007, Laupland *et al.* 2007) to calculate their incidence or prevalence.

During the study period (2010–2012), around 15–18% of the elderly patients visited their GP three or more times a year for UTIs (for the exact number see Appendix 18). This high number of visits might suggest that there was a high rate of UTI recurrence, which is very common in elderly patients owing to several factors such as existence of co-morbidities, weakened immune system and ageing itself (Nicolle 2005, Caljouw *et al.* 2011). Another explanation might be that patients might have received ineffective antibiotics, have been exposed to a multi-drug resistance pathogen, which can be common in elderly patients as a result of ageing and frequent exposure to antibiotic therapies, as shown by (De Vecchi *et al.* 2013), who found that bacterial resistance to antibiotics was rather widespread in elderly patients and that it may be responsible for antibiotic therapy failure in this population, or may not have adhered to antibiotic treatment. Each of these visits resulted in at least one antibiotic being prescribed for UTI.

In this DUR study, 37,815 (48.9%) of the total recorded UTI events in the IMS-DA ended with at least one antibiotic being prescribed. The general trend of antibiotics prescribing decreased with advancing age both annually as well as over the whole study period (2010–2012). However, this does not support the results of Pan *et al.* (2011), who reported the prevalence of antibiotics prescribing for the elderly to be 49% for those aged 65–74, 56% for those aged 75–84 and 69% for those aged 85 and over, or Haeseker *et al.* (2012), who reported a high rate of antibiotics prescribing in elderly patients that significantly increased over time with increase in elderly patients aged in particular 80 or older ($p <$ 0.001). There are several explanations for this. One is that Pan *et al.* (2011) and Haeseker *et al.* (2012) conducted their studies in the Netherlands and Italy respectively, two countries among those in the European Union with high antibiotics consumption and prescribing rates, particularly in the elderly (Adriaenssens *et al.* 2011, Haeseker *et al.* 2012). Another explanation is that elderly patients have the highest rate of antibiotics consumption in comparison with other age groups (Norris *et al.* 2011, Pan *et al.* 2011), largely because of their frequency of infection owing to weak immunity and worse general health (Htwe *et al.* 2007, Heppner *et al.* 2013). Yet another explanation is the inclusion into those studies of other infectious diseases such as RTIs without stratifying the consumption results per condition (Norris *et al.* 2011, Pan *et al.* 2011). A fourth might be the implantation of certain strategies or interventions to promote prudent use of antibiotics such as educational programmes, campaigns, audits and awareness programmes, which have been implemented in the UK since 1999 (Huttner *et al.* 2010, Harris 2013). In this study, perhaps, the reducing rate of antibiotics prescribing for UTIs with advancing age could be owing to the increase in the death rate among the elderly patients registered with the surgeries from which the data were obtained (ONS 2012). Another possible reason could be the increase in the total number of elderly population in the UK (ONS 2015a), which in turn might reflect on the total number of elderly patients who visit GP surgeries. A final explanation might be that some elderly patients moved from one catchment area to another and therefore followed up with a different GP whose records were not included in the IMS-DA.

In this study, trimethoprim was the most commonly prescribed antibiotic, with 15,772 (41.7%) prescriptions. This is consistent with the general result of Petersen and Hayward

(2007), who reported trimethoprim to be the most commonly prescribed antibiotic for UTI with a total of 25,147 (56.1%), and the female-specific results of Leistevuo *et al.* (1997), who reported either TMP-SMX or trimethoprim in 94 cases (37%), but not with the results of Friis *et al.* (1989), who found sulphamethoxazole to be the most commonly prescribed antibiotic in 1989. Sulphamethoxazole might have been effective in 1989 but not anymore because of the increased ADRs associated with it (Bendall 1984). Straand *et al.* (1998), Kahan *et al.* (2005), Taur and Smith (2007) and McIsaac *et al.* (2008) reported TMP-SMX to be the most commonly prescribed antibiotic for UTIs while the rest reported other antibiotics as the most common such as quinolones, pivmecillinam, fosfomycin and co-amoxiclav. A possible explanation for this variation in antibiotics prescribing for UTIs is variation in bacterial resistance, especially for *E. coli.*, which was considered to be the main infective pathogen responsible for the majority of UTI cases in elderly patients with increased resistance to many antibiotics that may also vary between countries as shown in a multi-country study of 908 *E. coli* urine cultures from Austria, Greece, Portugal, Sweden and the UK. The results showed different rates of *E. coli* resistance for different antibiotics including trimethoprim, co-amoxiclav, TMP-SMX, nitrofurantoin and ciprofloxacin (Kahlmeter and Poulsen 2012). Further, WHO global surveillance reported *E. coli* resistance of more than 50% of commonly used antibiotics, particularly fluoroquinolones and third-generation cephalosporins, which might make effective treatment of UTIs differ from one country to another based on resistance patterns (Aarestrup *et al.* 2014). Other possible explanations for this variation in antibiotics prescribing could be variations in first-line recommendations, for example, fosfomycin in Spain (Llor *et al.* 2011) versus nitrofurantoin or trimethoprim in Ireland (Vellinga *et al.* 2011), different geographical areas and cultures such as Ireland (Vellinga *et al.* 2011) versus the USA (Taur and Smith 2007), availability of antibiotics such as fosfomycin in Spain (Llor *et al.* 2011) but not in the UK, and antibiotics purchasing without a prescription from a GP, that is, self-medication as in Spain.

Nitrofurantoin was found to be the second most commonly prescribed antibiotic for elderly patients with UTIs, with 9,448 (25%) prescriptions. This result was consistent with the findings from Kahan *et al.* (2005), who reported nitrofurantoin prescriptions in 11,888 (18.51%) UTI cases in line with the diagnosis and treatment of uncomplicated UTI guidelines, and also from Denes *et al.* (2012), who found nitrofurantoin to be the second most commonly prescribed antibiotic based on urine analysis. Furthermore, nitrofurantoin was reported to be the third most commonly prescribed antibiotic in studies of elderly patients only (Taur and Smith 2007, McIsaac *et al.* 2008) and of all age groups and genders except males aged 80 and older (Haasum *et al.* 2013). In Petersen and Hayward (2007) nitrofurantoin was found to be only the fourth most commonly prescribed antibiotic for UTIs, possibly because the study used UTI patients' records without taking into consideration the influence of age, gender or UTI type. Overall, the prescription of nitrofurantoin for elderly patients may be associated with less compliance since it needs to be taken four times daily, making it less practical for the elderly. Additionally, it might not be used for patients with renal impairment, which is common in elderly patients for many reasons such as ageing-associated changes in the kidneys (Čukuranović and Vlajković 2005, Macias Nuñez *et al.* 2008) or as a result of drug–drug interactions as shown in Table 7 in Chapter One (Nicolle 2009a).

Only 1,617 (38.9%) antibiotics in females and 85 (54.1%) in males were found to be in line with the SAPG good practice points for LUTIs; while nitrofurantoin was prescribed appropriately for 190 (8.9%) female patients and 49 (50%) male patients with LUTIs. Overall, 9,125 (24.1%) prescriptions in this study were for broad-spectrum antibiotics. Among these broad-spectrum antibiotics, cephalexin was the most commonly prescribed in both genders (N = 5,042; 13.3%), followed by co-amoxiclav (N = 2,350; 6.2%) and ciprofloxacin (N = 1,733; 4.6%). The use of broad-spectrum antibiotics may increase the susceptibility of elderly patients to infections such as *Clostridium difficile*, which may lead to death (Beckett *et al.* 2015). Additionally, 12,159 (32.2%) of antibiotics prescriptions were for durations other than those recommended for treatment or prophylaxis; this was seen in 10,605 (33%) female and 1,554 (27.5%) male cases. Also, 4,416 (28%) trimethoprim prescriptions and 4,771 (50.5%) of nitrofurantoin prescriptions were for longer durations than those listed by the SAPG good practice points (SAPG 2013). These exposed elderly patients to inappropriate courses of antibiotic therapy, which consequently might have deteriorated their condition, caused ADRs and increased or developed bacterial resistance. Overall, the results from this DUR study in terms of comparing GPs' prescribing practices with SAPG good practice points indicated that there is some lack of adherence to recommendations as well as inappropriate antibiotics prescribing in terms of antibiotic choice and/or duration of therapy. In this DUR study, inappropriate prescribing was seen in the form of using broad-spectrum antibiotics and prescribing for inappropriate durations. These results support Straand *et al.* (1998), Kahan *et al.* (2005), Llor *et al.* (2011), Vellinga *et al.* (2011), Denes *et al.* (2012) and Haasum *et al.* (2013), who all reported either a lack of or poor adherence to guidelines on the part of

GPs and primary care physicians when prescribing for the adult population in general or for the elderly population in particular. However, these findings might not represent the true adherence of GPs to guidelines as GPs might deviate from the recommendations for antibiotics prescribing if urine sample results show resistance bacteria or if the patient has a reason that makes first-line therapy inappropriate such as co-morbidities, drug–drug interactions or ADRs in particular studies that based on computerised databases such as (Wrigley *et al.* 2002, Kahan *et al.* 2005, Petersen and Hayward 2007a, Taur and Smith 2007, Haasum *et al.* 2013).

## 4.4 Future Research

This quantitative, retrospective, observational, cross-sectional study was designed to explore GPs' antibiotics prescribing practice for elderly patients with UTIs over the three-year period 2010–2012. The results suggest the presence of some variations in GPs' antibiotics prescribing practice as well as non-adherence to SAPG good practice points in the forms of using broad-spectrum antibiotics and prescribing for longer durations. In order to understand whether these prescribing variations and none-adherence were resulted from IMS-DA data limitations such as lack of patients' social, clinical characteristics and compliance data or owing to presence of prescribing variation by GPs, future research should focus on exploring the phenomenon of how GPs prescribe antibiotics for elderly patients with UTIs. This future work needs to investigate whether there are variations in the way GPs approach, perceive and view antibiotics in this particular circumstance. Since this work will require in-depth description of GPs' thoughts, ideas, concepts and views, and because it will focus on describing this phenomenon in its natural context, qualitative research using a phenomenographic method might be appropriate.

## 4.5 Summary

In summary, this chapter presented the key findings for quantitative study related to GPs' antibiotics prescribing for elderly patients with UTIs. The results from the study were presented in the form of prevalence, tables and bar charts. The results suggest high prevalence of UTIs in elderly female patients compared with elderly male patients. With regard to GPs' antibiotics prescribing practice, the results suggest that some GPs' prescribing was not in line with the available good practice points.

# Chapter 5 Phenomenographic Approach for the Variations in GPs' Views and Perceptions about Prescribing Antibiotics for UTIs in Elderly Patients and Factors Influencing GPs' Antibiotics Prescribing for UTIs

This chapter presents the key findings and discussion about GPs' prescribing of antibiotics for elderly patients with UTIs who visited GP surgeries, from qualitative perspectives using phenomenography as methodological approach. The chapter discusses and interprets the findings and compares them with the findings from the relevant reviewed literature in Chapter Two. Since the data were allowed to stand on their own, without interpretation, they were discussed separately and without speculation about their meaning or trying to *'get inside the head'* of the GPs and somehow *'interpret'* what they meant. Should the findings suggest concepts that were not addressed in Chapters One and Two, the researcher might need to include a concise description before discussing the findings (Burnard 2004, Burnard *et al.* 2008).

## 5.1 Findings from Phenomenographic Analysis of Variations in GPs' Views and Perceptions about Prescribing

### 5.1.1 Introduction

This section presents the key findings from interviews with GPs about phenomenon of antibiotics prescribing for elderly patients with UTIs. The first part of this section discusses in detail the categories of description, including referential and structural components, that were identified by the researcher in the course of the interpretative analysis of the data. The second part of this section encompasses the diagrammatical presentation of findings outcome space.

### 5.1.2 Number of Interviews and Participants' Characteristics

Twenty GPs expressed their interest in participating in the research. Two GPs were located outside the Greater London Area; therefore, they were excluded. One GP out of the remaining 18 withdrew because of unavailability within the proposed research time frame. The final number of participants was 17 with no further withdrawals. Out of the 17 GPs, (N = 9; 53%) were female GPs. GPs mean age was 41.12 ± 9.94 and the average length for interviews was 68 minutes. Table 31 summarises participants' demographics and practice details.

Table 31: Summary of interviewed GPs demographics and administrative data

| GP code | Gender | Age (years) | Training Country[β] | Years of practice | Working days* | Average patients[§] | Duration of consultation[a] | Length of interview[a] |
|---|---|---|---|---|---|---|---|---|
| GP1 | F | 46 | Tanzania | 24 | 5 | 40 | 10-15 | 71 |
| GP2 | M | 58 | NA | 29 | 6 | 40 | 10 | 42 |
| GP3 | F | 35 | Various | 5.5 | 2 | 25-30 | 15-20 | 63 |
| GP4 | F | 33 | NA | <1 | 3 | 30-35 | 10-15 | 72 |
| GP5 | M | 45 | Ireland | 9 | 5 | 40-50 | 8-10 | 43 |
| GP6 | F | 40 | NA | 12 | 2/3 | 28 | 10 | 56 |
| GP7 | F | 37 | NA | 6 | 2.5 | 24-28 | 15 | 57 |
| GP8 | M | 36 | Australia/ New Zealand | 2 | 3 | 36 | 10 | 92 |
| GP9 | F | 30 | NA | 2 | 5 | 40 | 10 | 90 |
| GP10 | F | 33 | Zambia | 2 | 3 | 36 | 12 | 72 |
| GP11 | M | 50 | NA | 22 | 5 | 30 | 10 | 55 |
| GP12 | F | 35 | Malawi | 5.5 | 3 | 45 | 10 | 55 |
| GP13 | M | 45 | NA | 18 | 4 | 30 | 12 | 95 |
| GP14 | M | 34 | NA | 5 | 2 | 45 | 10-12 | 81 |
| GP15 | F | 33 | NA | 3.5 | 4 | 40 | 10 | 88 |
| GP16 | M | 42 | NA | 4 | 5 | 40 | 10 | 61 |
| GP17 | M | 67 | NA | 14 | 6 | 30 | 15 | 68 |

*per week; [§]per day; [a]minutes; [β]in addition to UK; F: Female; M: Male; NA: Not Applicable

### 5.1.3 Categories of Description of GPs' Views and Perceptions

Analysis of the 17 GP interviews resulted in identifying five distinctive categories of description representing the ways in which GPs perceive antibiotic prescribing in elderly patients with UTIs. These categories were:

- Perceptions;
- Knowledge;
- Decision;
- Practice; and
- Approach.

Findings in this section are presented as categories of description that represent the GPs' conceptions of experiencing the phenomenon of antibiotics prescribing for elderly patients with UTIs. Here, each of the five distinct categories of description consists of different dimensions, or subcategories, that represent a view or a perception shared by a group of GPs. It is important to stress that whether GPs experienced, viewed or perceived prescribing antibiotics for elderly patients with UTIs positively or negatively was not what was of import; it was how GPs perceived antibiotics prescribing in elderly patients as it was described in each category in the GPs' practice world. Each of these categories described below. Figure 29 summarises the five categories of descriptions and the dimensions from the phenomenographic analysis of the GP interviews.

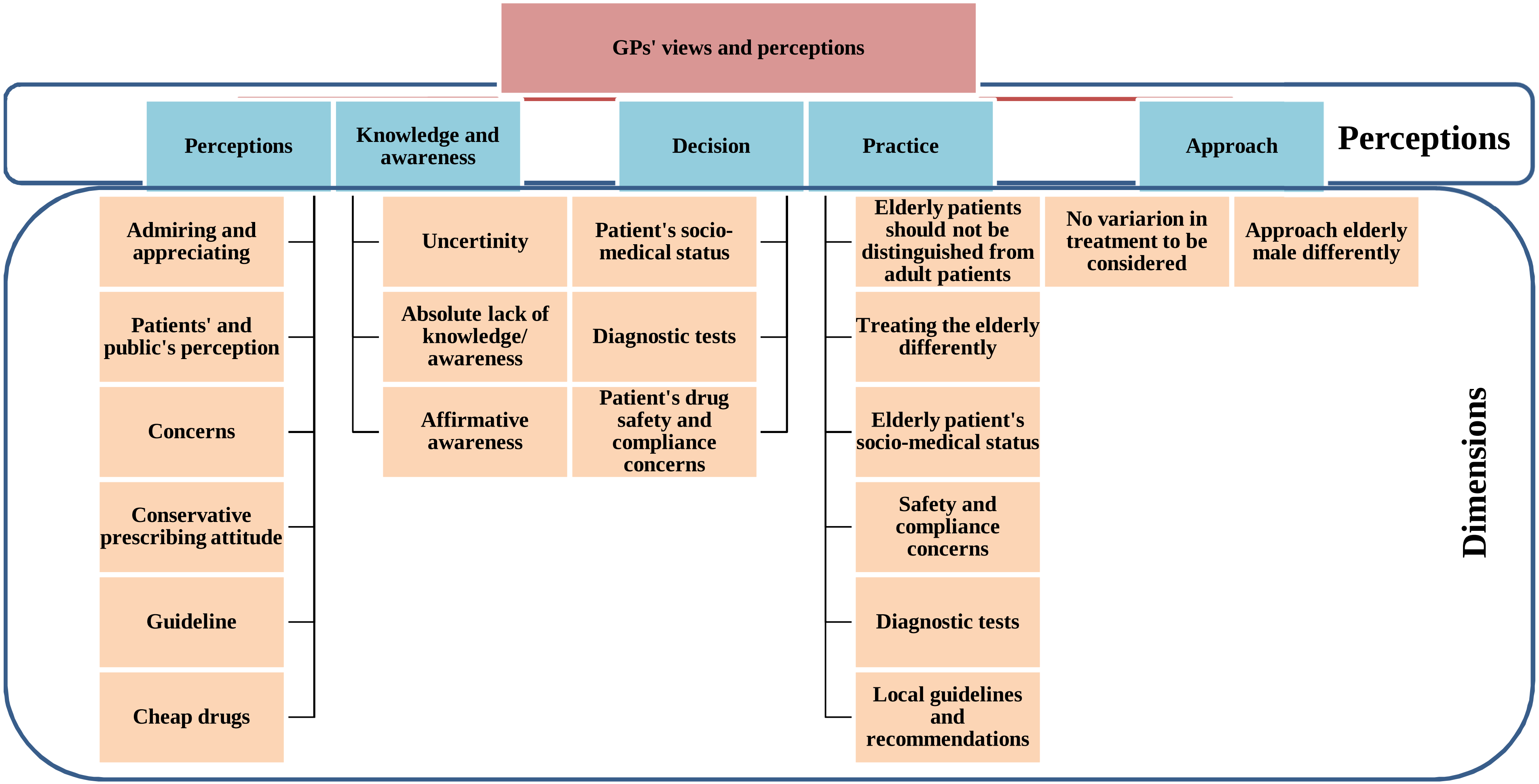



Figure 29: Summary of the five categories of descriptions and the dimensions from the GP interviews phenomenographic analysis

#### 5.1.3.1 Category of Description 1: Variations in GPs' Antibiotics Prescribing Perceptions

In this category of description, the way in which GPs perceived antibiotics as a group of drugs was described as perceptions. Data analysis revealed six different subcategories of admiring and appreciating the therapeutic value of antibiotics, patients' conceptions, concerns, conservative prescribing attitudes, guidelines and being cheap drugs. The following section explores in detail each of these dimensions of perceptions that emerged from the participants' answers. Findings are presented with explanations of each dimension supported by participants' quotes.

##### *5.1.3.1.1 Admiring and Appreciating*

In dimension 1 (admiring and appreciating), the majority of GPs (N = 15) focused on the therapeutic value of antibiotics, being one of the greatest innovations of this century and capable of saving patients' lives if used appropriately to treat bacterial infection. Moreover, participants admired the role of antibiotics in daily practice and the way antibiotics have revolutionised current medical practice. Participants used different words to describe their admiring perceptions of antibiotics, for example, *'life-saver'*, *'vital'*, *'crucial'* and *'important'*. Below are quotes by some participants to illustrate how they admired and appreciated antibiotics as a group of drugs:

> *'They're obviously effective. It's revolutionised patient care and health and life expectancy. People used to die of bacterial infections and they don't now. They're hugely important and they save lives … They're hugely important, hugely effective.'* **(GP6: 40, female, 12 years)**

> *'Wow. My perceptions are that when used appropriately they are wonderful because we have an unwell situation, a condition that can be treated to what … in essence is a cure. We don't have many cures in medicine so treatment of infection is fantastic.'* **(GP7: 37, female, 6 years)**

This participant described antibiotics as being the discovery of the millennium owing to their value in curing and saving millions of patients' lives. He could not imagine the world without them as they are the only group of drugs that can be used in any branch of medicine:

> *'I think they're lifesavers. Without antibiotic, millions and millions of people are dying. I cannot myself imagine the life pre-antibiotics, lots of people are dying for very, very small little infection … I cannot really believe that any medication in the whole world has affected human life as much as antibiotics. I think that if somebody asked what would be the discovery of millennium, I would say antibiotic*

> *and don't forget antibiotic is the only medication that is used by any branch of medicine.'* **(GP17: 67, male, 14 years)**

Another participant described with an example from their own practice how an appropriate course of antibiotics had saved an elderly patient's life after the patient was ill:

> *'I think that antibiotics when used appropriately can have a very marked effect especially on the elderly patient so I can think of numerous examples where I've seen a patient. He's been really off legs, really struggling and a few days later with a course of trimethoprim is significantly better'* **(GP4: 33, female, less than a year)**

##### *5.1.3.1.2 Patients' and the Public's Perceptions*

In dimension 2 (patients' and the public's perceptions), a group of participants (N = 4) focused on patients' perceptions, using utterances such as *'people'*, *'patient'* and *'public'*. Their perceptions were discussed from a dimension relating to patients' and the public's expectations, demands, misconceptions and beliefs about antibiotics. The following are quotes by participants that demonstrate the patients' and the public's perspectives on antibiotics.

This participant considered patients' expectations of antibiotics as well as their lack of understanding about the microbial activity of antibiotics as major problems encountered by GPs, since people do not understand the negative impact of improper use of antibiotics, which is that it can result in AMR:

> *'Patient expecting antibiotics ... Unfortunately, that's one of our biggest problems with antibiotics, is that people don't understand that they only work against bacterial infections and if you have a viral infection… they're not going to work and actually they're dangerous, because they can mean the bugs start to mutate and our antibiotics that we have don't work anymore. I don't know if people understand that in general really, I would say not in my population anyway.'* **(GP6: 40, female, 12 years)**

This participant described how patients come to see her with the aim of getting an antibiotics prescription and explained her own interpretation of this behaviour by the public and patients:

> *'I guess another perception is that people want them, so people often come to see me with the sole aim of obtaining an antibiotic. And I guess the perception is that the public want… desire antibiotics and think that they're very helpful drugs.'* **(GP9: 30, female, 2 years)**

The quote given here explains how GPs' perceptions about antibiotics can differ from patients' perceptions, focusing on those who consider antibiotics to be a fix for all medical problems:

> *'I think that there is a perception that other people have, that sometimes they can fix everything… Often patients seem to think that one antibiotic will solve all kind of what you think need antibiotic themselves and solve this problem which I have, whatever their problem they have. The patient's perception of how they work, is not the same as our perception and our impression of how they work and how they can be used… I think some people over use, potentially, but probably on the basis that they are being asked for them.'* (**GP10: 33, female, 2 years)**

### *5.1.3.1.3 Concerns*

Dimension 3 deals with (concerns), focusing on patient safety, microbial resistance, lack of antibiotic effectiveness and cautious use of antibiotics. The majority of participants who addressed this perception (N = 14) used terms such as *'side effects', 'problem', 'worry' and 'cautious'* to describe their concerns in delivering this insight.

This participant revealed the culture of awareness among GPs with regard to AMR, which can be a consequence of inappropriate antibiotics use:

> *'Absolutely have their uses and need to be used appropriately. I think there's an increasing awareness among general practitioners that these need to be used appropriately but not abused because of the emerging resistance, as I was saying.'* **(GP12: 35, female, 5.5 years)**

This quote, on the other hand, suggests that the lack of development of new antibiotics in the last 20 to 30 years has contributed to the increase in AMR and created a status of selective pressure. This caused him deep worry should the world ever reach the stage of a post-antibiotic era:

> *'There not being any antibiotics for 20 to 30 years means we've got increasing resistance and selective pressures because of mutations of bacteria. So that's a real big worry of mine that, and also the Chief Medical Officer as well in the UK and internationally in the World Health Organisation talked about a post-antibiotic world where antibiotics will cease to be effective for many common conditions. So, that's a worry for me within my lifetime, that could these commonly used drugs which generally still work for most bacterial infections, maybe they might not be effective, and that'd be a quite scary thought, to see patients might start dying again more commonly having bacterial infections that could potentially harm patients. That's a quite scary thought.'* **(GP14: 34, male, 5 years)**

Another prime concern by participants was related to the side effects of antibiotics. One GP associated these with antibiotics administration and the word 'horrible', and said it had a tendency to limit her prescribing to indicated cases only:

> *'A lot of antibiotics have horrible side effects like nausea, and diarrhoea, and all the common antibiotic side effects'* **(GP15: 33, female, 3.5 years)**

Strong concerns about side effects were unveiled by the majority of the interviewed GPs:

> *'I guess I perceive that they are quite high in terms of side effect risk, so I really pretty much expect a patient to have side effects when I give them an antibiotic and I will tell them that. You know gastrointestinal upset or rashes or just not feeling very well with them.'* **(GP9: 30, female, 2 years)**

In the following quotes, participants highlighted problem of some GPs over-prescribing antibiotics, which can result in reduced or lack of efficacy as well as the spread of bacterial resistance:

> *'All know, they're over-prescribed and this led to lots of problems with resistance, reduced efficacy, MRSA and things like that…but as I said, the rise of antibiotic prescribing has led to problems of resistance and unnecessary prescribing.'* **(GP6: 40, female, 12 years)**

> *'I think probably the use of them is ... we over-prescribe them, definitely; and for lots of the conditions that we prescribe them for, it's probably not going to add a huge amount of benefit because there's more and more evidence coming out that antibiotics will only shorten an illness by a few hours, for example, and therefore overall, they don't offer that much benefit.'* **(GP9: 30, female, 2 years)**

***5.1.3.1.4 Conservative Prescribing Attitudes***

In dimension 4 (conservative prescribing attitudes of GPs), few participants (N = 3) showed a conservative attitude towards antibiotics prescribing. Participants used utterances such as *'reluctant' and 'failure of them'*. Participants tended to be conservative when there was no definite indication or because they preferred to encourage the use of over-the-counter (OTC) or non-pharmacological choices as an alternative before prescribing an antibiotic. The following quotes by participants help to explain the motives behind their conservative behaviour:

> *'If somebody has a UTI, then if it's symptomatic, it should be treated. Sometimes self-treatment works ... treatment with over-the-counter preparations and by drinking plenty. Often it doesn't work, and particularly if there's been a failure of self-treatment, then it's very reasonable to use a course of antibiotics.'* **(GP2: 58, male, 29 years)**

> *'Personally, I wouldn't want to take antibiotic unless I was on death's door … I think I'm reluctant to give them unless I think they definitely have got something that needs treating.'* **(GP15: 33, female, 3.5 years)**

***5.1.3.1.5 Guidelines***

Participants (N = 3) in dimension 5 (GPs influenced by guidelines) viewed antibiotics from guideline perspectives, using utterances such as *'guideline' and 'guidance'* to express this perception. Participants used guidelines either to explain to patients how diagnosis and/or management work or to discuss how adhering to guidelines had a positive impact on the practice.

This participant described how adherence to guidelines reflected on the prescribing practice in the surgery where she works:

> *'I can comment heavily on the practice in how doctors practice in my practice …, I'm very pleased because we adhere to the local guidance of what microbiology have said, 'Okay, this is first-line for this,' or if there isn't that guidance, whatever the local or the national guidance is.'* **(GP7: 37, female, 6 years)**

One participant provided a scenario about their current practice in the case of a patient with a UTI and how her awareness of the guideline recommendations was incorporated into the process of diagnosis and management:

> *'If I see a young person and they're well, I'm quite happy to send off. It's not cut and dry whether they've got a UTI or not, and they're really quite well, then I'll say, 'Well, we could just send of a urine sample and then see the results.' If they've got classic symptoms, NICE guideline say's if they've got clear cut symptoms, then just treat them. Don't even send an MSU.'* **(GP12: 35, female, 5.5 years)**

#### *5.1.3.1.6 Cheap Drugs*

In dimension 6 (GPs perceiving antibiotics as cheap drugs) a group of participants (N = 3) perceived antibiotics from an economic standpoint. Participants used utterances such as *'cheap' and 'cost'* as well as monetary terms to elaborate on this perception. This participant's quote provides an illustration of how antibiotics are perceived as cheap drugs compared with others:

> *'I guess I perceive that they're fairly cheap in terms of the medications that we prescribe, so I guess from a cost-effective point of view, they are fairly cost-effective because often the prescription is only a few pounds rather than more expensive than that.'* **(GP9: 30, female, 2 years)**

Another two participants estimated the cost of antibiotics to range from pennies to a few pounds. The two quotes demonstrate how participants undervalue the economic cost of antibiotics when prescribing them since the cost of acquiring antibiotics is cheap compared with other drugs:

> *'Because they're so cheap, just a penny.'* **(GP17: 67, male, 14 years)**

> *'They're very cheap. It's like a pound here, a pound there.'* **(GP14: 34, male, 5 years)**

### 5.1.3.2 Category of Description 2: Variations in GPs' Knowledge and Awareness of UTI Guidelines

This category described how aware GPs were of available recommendations and guidelines with regard to the treatment of UTIs with antibiotics in elderly patients, in particular the SAPG good practice points. In this category, participants gave different responses that indicated the presence of variations in the level of awareness about the status of specific recommendations or guidelines for elderly patients with UTIs. Perceptions from participants ranged from uncertainty about the availability of such recommendations and guidelines, to absolute lack of awareness of specific guidelines in some cases and confident awareness of recommendations and guidelines specifically for elderly patients in others.

#### *5.1.3.2.1 Uncertainty*

In dimension 1 (uncertainty), some participants (N = 6) expressed their uncertainty about the availability of recommendations and guidelines using phrases such as *'I'm not sure', 'I don't think' and 'I don't remember'*. In fact, participants who expressed uncertainty seemed shy or surprised when giving their answers. Moreover, they were curious to know if there are any guidelines.

This participant was surprised by the question about her awareness of any specific guidelines or recommendations for UTIs in elderly patients and she expressed her uncertainty by answering the question in a very confusing way:

> *'Oh my gosh. Sorry. That is a good question. No. I don't think I am actually. I probably should be. I should know it. Now you've mentioned it I think there is. In this envisaging the guidelines we have which is sort of several pages of very small text. I think there probably is. Yes, I think there are recommendations. I don't think I've reviewed them recently and probably should do.'* **(GP4: 33, female, less than a year)**

Another participant used the word 'silly' to describe her feelings of uncertainty about the availability of such recommendations:

> *'Well, I don't know any names of any. I bet you there are some that exist and I feel very silly now so I don't know of any.'* **(GP7: 37, female, 6 years)**

Two more participants expressing their uncertainty about the existence of guidelines and recommendations related to this topic:

> *'No. I don't remember seeing any specific... There must be really. I can't think of any specific guideline.'* **(GP13: 45, male, 18 years)**

> *'Maybe there is, yeah. I'm not aware of that. Maybe there is. Is there?'* **(GP8: 36, male, 2 years)**

### *5.1.3.2.2 Absolute Lack of Knowledge/Awareness*

In dimension 2 (absolute lack of knowledge/awareness of guidelines and recommendations relating to UTIs), the majority of participants (N = 8) expressed complete lack of awareness and knowledge of any specific recommendations or guidelines by using phrases such as *'We haven't' and 'I'm not'*. Within this dimension, some participants highlighted the availability of recommendations and guidelines for UTIs in adults but were not aware that they distinguish between adults and the elderly. Furthermore, participants tried to justify their position without giving reasons for their lack of awareness. Again, as in the previous dimension, participants with this perception were curious to know whether there are any recommendations or guidelines for this subject.

This quote illustrates the participant's opinion that it was unnecessary to justify being aware of asymptomatic UTI recommendations relating to the elderly but not other UTI guidelines. The participant expressed their curiosity about whether any such guidelines or recommendations exist for elderly patients with UTIs:

> *'I have to confess that no I'm not on any specific ones, no. I am aware of discussions about symptomatic and asymptomatic UTIs and that you shouldn't be treating asymptomatic UTIs, but your question is about symptomatic UTIs. In which case I confess I don't. You can tell me about them afterwards'* **(GP3: 35, female, 5.5 years)**

The following quote demonstrates the same ignorance of any specific guidelines or recommendations and the same conviction that justification of the lack of awareness is unnecessary, as well as wondering if any new guidelines on the topic are available:

> *'Interesting. I cannot… we haven't any specific ones, because our local hospital hasn't actually issued us any specific guidelines. But you're whetting my appetite, and I'm sort of thinking maybe NICE has come up with some recommendations or DoH has.'* **(GP11: 50, male, 22 years)**

These two participants, with more than 20 years' practice experience each in addition to their academic background, shared the same lack of awareness of any recommendations or guidelines:

> *'For older people, no…Not specific for older, no.'* (**GP1: 46, female, 24 years)**

> *'Not specifically for elderly, no.'* **(GP2: 58, male, 29 years)**

#### *5.1.3.2.3 Affirmative Awareness*

Contrary to the previous subcategory, dimension 3 (affirmative awareness) saw a group of participants (N = 3) answering this question with confidence and revealing an affirmative awareness of specific guidelines for elderly patients with UTIs. These participants used *'there is'* to support their view. The following quotes from three participants with between four and 14 years of practice experience describe their confident awareness of specific guidelines for elderly patients with UTIs:

> *'There's a NICE guidance on UTIs in general. It mentions elderlies as a part of that…The NICE guidance on urinary tract infections.'* **(GP12: 35, female, 5.5 years)**

> *'Yes…It's community guidelines from the local pharmacists and they do it in collaboration with NICE. Last reviewed in April 2013…It's not changed. The last time I looked at it is maybe once or twice a year to see if there's any differences.'* **(GP16: 42, male, 4 years)**

> *'Yes, there are. There's NICE guidelines just UTI in elderly people and the treatment of UTI. They are NICE guideline; you choose the most important one'* **(GP17: 67, male, 14 years)**

### 5.1.3.3 Category of Description 3: Variations in GPs' Decision to Treat

This category focused on important variations in GPs' often challenging decision to treat elderly patients with UTIs. Data analysis revealed three distinctive and varied perceptions with numerous factors that may influence the participants' decision to treat elderly patients with UTIs, including the patient's socio-medical status, diagnostic tests and safety and compliance.

#### *5.1.3.3.1 Patients' Socio-medical Status*

In dimension 1 (patients' socio-medical status), all participants (N = 17) perceived patients' living status or presence of a person to take care of them, current symptoms and clinical presentation, previous UTI episodes, UTI recurrence and co-morbidities as main factors on which to base the decision to treat elderly patients with UTIs. Utterances such as *'co-morbidities'*, *'history'*, *'examination'*, *'living'* and *'alone'* were used to highlight this view.

The following four quotes illustrate how important it is for GPs to consider elderly patients' living status when deciding to treat them:

*'I would also be looking at, if they lived alone at home, all of those things would have an impact on my decision to prescribe or not.'* **(GP1: 46, female, 24 years)**

*'Are they unwell, what are the social circumstances?'* **(GP6: 40, female, 12 years)**

*'Are they alone or they've got people caring for them who will be able to call someone quicker?... Are they housebound?.'* **(GP12: 35, female, 5.5 years)**

*'Whether the patient living alone, can somebody give the medication on time… It's a social situation with the patient.'* **(GP17: 67, male, 14 years)**

These participants discussed patient medical history and examination as an influential factor in their decision to treat:

*'The history, examination, whether the patient has got a fever, got significant abdominal pain and severity of the symptoms, have they had a fall, confusion, delirium, so all of those things would mean that I would treat the patient.'* **(GP8: 36, male, 2 years)**

*'Basically history and story that they've told me and examination. Although we might not expect to find much on clinical examination if it's UTI. Making sure that it isn't something else.'* **(GP10: 33, female, 2 years)**

These participants perceived the decision to treat elderly patients with UTIs from a symptoms-focused perspective:

*'I guess whether they present with urinary symptoms, or you want to check whether they've got dysuria, frequency, urgency, poor flow, seen blood, then whether they've actually got pain suprapubic pain. Whether they've got any sense of renal involvement, they've got groin pain, checked their observations, blood pressure, pulse, temperature, examine them. All those I guess will inform the decision.'* **(GP3: 35, female, 5.5 years)**

*'Mostly their symptoms. if someone's got very specific urinary symptoms, you know burning, go more often, then I'd be much more likely to prescribe rather than if they were just a bit non-specifically unwell and had a bit of a fall or something.'* **(GP15: 33, female, 3.5 years)**

#### *5.1.3.3.2 Diagnostic Tests*

Several participants in dimension 2 (diagnostic tests) (N = 9) viewed the decision to treat elderly patients with UTIs from a diagnostic perspective. Words such as *'diagnosis'*, *'MSU'*, *'urine analysis' and 'dipstick'* were used extensively during the interviews. Participants based the decision to treat on diagnostic tests, by requesting a urine sample for MSU or a urine dipstick test, as is shown in the following two quotes:

*'It might be reasonable to do an MSU ... the urine test .... and then only treat on the basis of that MSU.'* **(GP2: 58, male, 29 years)**

> *'Obviously then you do a urine analysis and dipstick it. If there's nitrites, definitely, but a lot of the time it's not nitrites. A lot of the time you just see leukocytes or some blood, but I think if there's blood and leukocytes then I normally do still treat and then I send of the MSU as well… I think I always send an MSU off'* **(GP3: 35, female, 5.5 years)**

A third participant stressed heavily that they requested a urine sample from the patient where possible, upon which to base the decision to treat:

> *'I would want a sample. I'd want a dip, a sample. And it would be based on that, that I would decide what to do… Where possible, I would always want a sample.'* **(GP10: 33, female, 2 years)**

This participant explained how their decision to treat elderly patients with UTIs was mainly based on the result of urine dipstick tests that he often requested:

> *'If the urine dips are showing nitrates and they're not catheterised, I'm likely to start them on the antibiotics. If it's showing leukocytes… essentially, I do the urine dip. I do that on most of my patients.'* **(GP16: 42, male, 4 years)**

#### *5.1.3.3.3 Patients' Drug Safety and Compliance Concerns*

Dimension 3 (patients' drug safety and compliance concerns) focused on participants' perceptions relating to drug safety and compliance in elderly patients (N = 4). Utterances such as *'take', 'interaction' and 'compliance'* describe this view, as illustrated by the following quotes:

> *'Are they likely to take the medicine? Are they able to take the medicine? Cause of course with elderly patients often you have to consider doing it to get district nurses in to supervise the medication and then the dosing of that… Particularly for instance I now prescribe nitrofurantoin often in a BD basis rather than QDS basis because of that particularly because actually if the district nurse would come in twice a day and monitor that person taking that medicine, then that can be much more easily. Of course four times a day for district nurses is pretty much impossible.'* **(GP4: 33, female, less than a year)**

> *'Look at their allergies, look at what other medications they're on, look at interactions, then you make a decision about which antibiotic to give them.'* **(GP14: 34, male, 5 years)**

> *'Does she going to get the antibiotic on time, is she able to be compliant with the antibiotic'* **(GP17: 67, male, 14 years)**

### 5.1.3.4 Category of Description 4: Variations in GPs' Prescribing Practice

This category mapped the variations in participants' perceptions following the decision to prescribe antibiotics for elderly patients with UTIs. Interview analysis identified six qualitative characteristic dimensions. Elderly patients should not be distinguished from adult patients, treating the elderly differently, elderly patients' socio-medical status, safety and compliance concerns, local guidelines and recommendations and diagnostic tests.

### *5.1.3.4.1 Elderly Patients Should not be Distinguished from Adult Patients*

In dimension 1 (elderly patients should not be distinguished from adult patients), a group of participants (N = 6) centred their discussions on treating elderly patients with UTIs in a similar way to adult patients. They used phrases such as *'the same'* and *'I don't think'* in describing their practice in this vulnerable group. The following quotes by several participants illustrate this view:

> *'I don't think there would be huge variation between young and old people.'* **(GP8: 36, male, 2 years)**

> *'I guess whether it's young or old, if it's a suspected UTI, it's automatically something that is going to get an antibiotic.'* ***(GP9: 30, female, 2 years)***

This participant revealed his perception of treating elderly patients with UTIs using the same antibiotic and the same dose as for adult patients. Also, he perceived elderly patients as a subgroup of adults:

> *'We'll be using the same antibiotics by and large, which I've already mentioned the names of, anyway. The dosages of the medication ... you'd probably stick to a fairly standard dose of those as well…. I don't tend to think of the very elderly as a separate subgroup of patients for the UTIs … It's more I tend to think of adults and the elderly as one group and children as the other group.'* **(GP11: 50, male, 22 years)**

### *5.1.3.4.2 Treating the Elderly Differently*

In dimension 2 (treating the elderly differently), several participants (N = 7) admitted to treating elderly patients with UTIs in a different way than they would treat adult patients. These participants tended to prescribe more antibiotics, to initiate antibiotic treatment earlier if possible or to use antibiotics with altered duration compared with adult durations owing to multiple factors such as frailty and fear of further complications. Participants used phrases such as *'treat early'*, *'more likely to treat'* and *'duration'*. Several quotes were used here to support this perception by different participants.

The following quotes describe how they initiate antibiotic therapy in elderly patients as early as possible because of frailty, risk of falling as well as confusion:

*'If they're quite frail, in order to prevent to come up falling, come up confused. I think there's a window of trying to start them on antibiotics and quite early.'* **(GP10: 33, female, 2 years)**

*'I think because elderly people can become more unwell with UTIs then we would probably, I think, we would probably treat them … be more likely to treat them rather than wait and see.'* **(GP13: 45, male, 18 years)**

Several participants expressed their tendency to prescribe antibiotics for elderly patients in terms of a low-threshold compared with adults:

*'I'm more likely to give them antibiotics in some ways, because this is someone who doesn't come in. So there is something a little bit of that, that which you're taught that people who rarely come in, and they're old, and they come in with something which might seem minor, you've just got to be a little more mindful and cautious about what that might mean.'* **(GP1: 46, female, 24 years)**

*'I think it's generally with elderly patients you might have a lower threshold for prescribing just to ensure safety because with elderly patients that's why you've got to be more mindful of things like Clostridium difficile and that sort of thing.'* **(GP4: 33, female, less than a year)**

Other participants tended to prescribe differently by prescribing antibiotics with different durations:

*'You want to give them a short course as possible.'* **(GP3: 35, female, 5.5 years)**

*'I think you're probably more likely to prescribe in the elderly and you more prescribe the longer courses as well, cause the standard course is three days for UTI. In the elderly, I know some people think you should give them a week's course of the antibiotics, so it might affect, there would be a number of medications you gave as well.'* **(GP6: 40, female, 12 years)**

*'It tends to be the duration of treatment which is different. I think ... I'm trying to remember the local guidelines from my head…. Okay. No, I think the only difference really would be the duration.'* **(GP15: 33, female, 3.5 years)**

#### *5.1.3.4.3 Elderly Patients' Socio-medical Status*

In dimension 3 (elderly patients' socio-medical status), participants (N = 4) stated that the treatment decisions were influenced by patients' socio-medical status when prescribing antibiotics for elderly patients with UTIs. The concept was reported in the form of determinants such as patients' living status, frailty and patients' co-morbidities.

These quotes from participants demonstrate the influence of elderly patients' socio-medical status as an explanation for the variations in antibiotics prescribing for elderly patients with UTIs:

> *'What the social situation is. Whether somebody's at home to care for them, look after them. Making fall back plans, so it's less about prescribing but more about the surrounding care and the safety netting of the patient.'* **(GP3: 35, female, 5.5 years)**

> *'Taking into account the … again, it's more co-morbidities…it's usually if there's diabetes or of the illnesses present'* **(GP7: 37, female, 6 years)**

In this quote, the participant explains comprehensively the differences in her perception with regard to treatment when she examines an elderly patient versus a young patient:

> *'I admit I've been more incline to give an elderly patient an antibiotic, particularly if they have co-morbidities like lung disease, ischemic heart disease, diabetes, because I want to give them the best possible chance of getting better. And If there is even a twenty percent chance this is bacterial, then it's worth giving them an antibiotic to be safe, I guess … there is also a perception that young people will always come back if they're not better. Elderly patients may be less likely to because they're house-bound or they have problems with contacting us because they have hearing problems or eyesight problems or don't want to bother the doctor.'* **(GP9: 30, female, 2 years)**

#### *5.1.3.4.4 Safety and Compliance Concerns*

In dimension 4 (safety and compliance concerns), safety was the main concept mapped from participants' interviews regarding variations in prescribing for elderly patients (N = 4). This was seen in various elements including interactions, side effects, appropriate dosing as well as patient compliance.

The following quote illustrates the participant's perception of safety and compliance in general and in elderly patients in particular:

> *'You have a much higher awareness of the safety and implications of prescribing things both in terms of drug interactions, allergies, side effects, all those kind of things. Obviously you're aware of all age groups, but particularly drug interactions because they're more likely to be taking other medications.'* **(GP12: 35, female, 5.5 years)**

Another two quotes are centred on safety from the perspective of drug–drug interaction in elderly patients:

> *'I guess I'm just more conscious about interactions with the drugs with the elderly, particularly with things like anticoagulants.'* **(GP3: 35, female, 5.5 years)**

> *'I'm just a bit more cautious about dosages and drug interactions than I might be with a younger person.'* **(GP15: 33, female, 3.5 years)**

The same participant expressed further concerns regarding safety by focusing on appropriate dosing in elderly patients with renal problems:

> *'I'm just a bit more cautious in terms of any dose changes that might be needed because of their renal function … I'd probably just check they didn't have any kind of renal impairment and things…. I just always be bit cautious with the dosing.'* **(GP15: 33, female, 3.5 years)**

Another participant perceived concerns about safety by considering appropriate antibiotic doses in elderly patients:

> *'I think one is the considerations of just making sure the doses are super correct because some have to be reduced. Renal function is checked.'* **(GP7: 37, female, 6 years)**

Compliance was another perception mapped by a few participants when deciding to prescribe antibiotics for elderly patients, as exemplified by these two quotes:

> *'You might want to issue a blister pack. You might want to check about issues around compliance.'* **(GP3: 35, female, 5.5 years)**

> *'Then again you're thinking more about compliance. Is he taking tablets, remembering to take them? Does it need to be added to a dosette or is this something that they're going to be able to take themselves? Those kind of things.'* **(GP12: 35, female, 5.5 years)**

#### *5.1.3.4.5 Local Guidelines and Recommendations*

In dimension 5 (local guidelines and recommendations), a few female participants spoke of adhering to and implementing recommendations. They used phrases such as *'local guidance'* during the interview. The following two quotes were extracted from interviewees who elaborated on their practice, which centred on adherence to local recommendations:

> *'Local guidance that we do have in terms of, okay, if you got a patient over 65, you can give this the first-line and it's for seven days and not three if it's a UTI, if it's a female.'* **(GP7: 37, female, 6 years)**

> *'I'd still go with the local guidelines or if they had a urine result that came back and the sensitivities didn't match with what they had already been given, I would still go with whatever drug was recommended but I would… unless it was absolutely contraindicated.'* **(GP15: 33, female, 3.5 years)**

#### *5.1.3.4.6 Diagnostic Tests*

Dimension 6 (diagnostic tests) included perceptions relevant to the use of diagnostic tests in the form of MSU, mainly, to confirm UTI infections for the purpose of prescribing (N = 3). Participants used *'MSU'* extensively to express these perceptions. The following quotes are illustrations of how participants perceived the role of diagnostic tests in elderly patients with UTIs:

> *'If somebody if the symptoms appeared mild ... if somebody was otherwise fit and well, if there was no clinical features of any complications, so no blood, no fever, no sign of kidney infection ... I suppose bladder infection ... then it might be reasonable to do an MSU ... the urine test .... and then only treat on the basis of that MSU.'* **(GP2: 58, male, 29 years)**

> *'I suppose the only thing with that UTI is that you have the benefit of an MSU that you can get more of an answer I suppose. You can also look back to see if somebody has had a problem with recurrent UTIs especially in elderly patient. You might have the benefits of looking back and seeing lots of positive MSUs in the past or a history of mixed bacterial growth with improvement in physical symptoms…. With UTI if you've got lots and lots of negative MSUs, you might be looking for another reason for symptoms rather than just carrying on prescribing antibiotics that's I suppose that's the only thing.'* **(GP4: 33, female, less than a year)**

This participant described in detail their own prescribing practice for elderly and adult patients and when they might request an MSU sample:

> *'A younger female with two-day history of dysuria and frequency and slight mild abdominal pain, I'll prescribe three days of trimethoprim. I probably wouldn't send off the MSU and so on in an uncomplicated UTI. Elderly patients I'll probably be more likely to send off an MSU.'* **(GP8: 36, male, 2 years)**

#### 5.1.3.5 Category of Description 5: Variations in Antibiotics Prescribing Approach for Elderly Patients with UTIs According to Gender

In this category, participants showed two different perceptions when they were asked whether they differentiated between males and females when prescribing antibiotic therapy for UTIs in elderly patients. The first group did not consider that gender was a factor and confirmed that both genders should be treated the same, whereas the second group of participants centred their approach on treating male and female elderly patients differently.

##### *5.1.3.5.1 No Variation in Treatment to be Considered*

In dimension 1 (no variation in treatment to be considered), participants (N = 7) expressed that elderly male patients did not necessarily differ from elderly female patients in terms of antibiotics treatment approach. Neither the antibiotic choice nor the duration needed to be changed in elderly male patients with UTIs when compared with elderly female patients. Utterances such as *'no difference'* were used to address this view.

This participant indicated no difference in relation to treatment although the process might be slightly different:

*'Probably no difference at all. I'm aware that the process is slightly different, and it's more prostate related in older men and common in older men and women, but both are vulnerable to septicaemia; both are vulnerable to kidney infection.* **(GP2: 58, male, 29 years)**

The quotes from these two participants demonstrate how their antibiotics prescribing for elderly males does not differ from their prescribing for elderly females:

*'When I am prescribing for old men versus old women for UTI there would be no major differences in my prescribing.'* **(GP4: 33, female, less than a year)**

*'It doesn't really. I don't think there's a huge amount of difference. I'm more likely to think about prostate problems in old men who get recurrent UTIs. Have they got some sort of obstruction? Are they emptying their bladder, that sort of thing. In terms of would I give them antibiotics or not, it's probably similar.'* **(GP12: 35, female, 5.5 years)**

### *5.1.3.5.2 Approach Elderly Male Patients Differently*

In dimension 2 (approach elderly male patients differently), just over half of the group (N = 10) expressed that they used different approaches when dealing with elderly males and females. Some reported a difference related to antibiotic choice, which may have been broader in its spectrum; others reported the use of the same antibiotic choice but with an extended duration of therapy.

This participant described her approach with the word *'aggressive'* in terms of the use of broader-spectrum antibiotics with longer duration for elderly male patients as compared with elderly female patients:

*'I'm a bit more aggressive with the men and I think the local guidelines I really should have checked them. I don't see it that often in a man, but usually a bit more aggressive in terms of antibiotics, so I give them a broader spectrum antibiotic I think for a longer period of time'* **(GP3: 35, female, 5.5 years)**

Several participants (N = 8) used the same antibiotic choice with a longer duration of therapy, as can be seen in the following quotes:

*'Well, obviously, it would be the duration, you know, you'd spend longer for men than women. But yeah, not the choice of the antibiotic per se, but the length of time.'* **(GP1: 46, female, 24 years)**

*'Well a man obviously quite different than females. So if a man is symptomatic he needs longer antibiotics.'* **(GP5: 45, male, 9 years)**

*'Well, in men, I tend to give a longer course of antibiotics. Say women, a three or five-day course. In men, we treat it for a bit longer. This is based on what? I knew you were going to ask about that. I mean, a lot of the implications' based on UTIs*

> *in women but there probably isn't any rationale to it but I would say in men, I'd probably give a seven-day course of antibiotics.'* **(GP13: 45, male, 18 years)**

The following two participants approached treatment of elderly male patients with UTIs differently, focusing on the choice of antibiotic drug:

> *'Old men versus old women? So in old men, the guidelines tell us, I think, to use cipro? Is that right? No. trimethoprim. Oh my God. Prescribing in men is different to women, in anyway. I think in men ... God, what do we do? trimethoprim, first line. And then we more likely to use things like ciprofloxacin in elderly men. But always seven days. Yeah. I think your choice of antibiotic might be slightly different in a man, but the duration will be the same'.* **(GP9: 30, female, 2 years)**

> *'I have worked in some places where they recommend Augmentin first line rather than trimethoprim or nitrofurantoin for men.'* **(GP8: 36, male, 2 years).**

### 5.1.4 Internal and External Horizons of GPs' Antibiotics Prescribing

The internal horizon of GPs' perceptions about antibiotics were discussed through GPs exposing and interacting with different factors and stakeholders including healthcare bodies, diagnostic and investigative processes, diseases, drugs, economics, GPs, patients and society. While knowledge of guidelines and recommendations for elderly patients with UTIs was mainly felt by participants to be related to GPs guidelines and the healthcare system, the treatment decision was experienced through considerations of multiple factors related to patients, diagnostics and investigation, GPs, diseases, guidelines and drugs. A variation in both the practice and the approach of antibiotics prescribing for elderly patients with UTIs was identified through participants' considerations including GPs, diseases, patients, gender, guidelines, diagnostics and investigation, and drugs. Figure 30 summarises the internal aspects of participants for each category of description.

Participants were aware of their perceptions, knowledge, decision, practice and approach in relation to what they were experiencing. The analysis revealed the presence of seven aspects that shaped and impacted participants' current understanding and practice in relation to this phenomenon under study, namely, undergraduate education, postgraduate training, interaction with peers, influence of patients, the healthcare system, GPs' personal experience, and the availability of guidelines and evidence. Figure 30 summarises the aspects of the external horizon as recognised from the participants' interviews. Participants described the aspects that shaped their intellectual understanding and impacted their practice by using different expressions, as shown by the following quotes:

> *'Because of the evidence, because of the evidence in the literature and talking to other people, talking to colleagues, but you're talking about the same evidence though. You're exchanging facts that come from literature.'*
> **(GP3: 35, female, 5.5 years)**

> *'Also feedback to the practice about prescribing patterns.'* **(GP3: 35, female, 5.5 years)**

> *'I think because of the nature of our practice and the type of patient that you might do that prescription for is often the kind of person you don't see regularly'* **(GP4: 33, female, less than a year)**

> *'I guess with increased experience; I've gained more knowledge of which antibiotic ... Which are appropriate for specific conditions.'* **(GP9: 30, female, 2 years)**

*'In medical school, we were taught a lot about side effects and risks and side effect profiles.'* **(GP9: 30, female, 2 years)**

*'I think really just working in a hospital. Seeing more patients. Seeing patients with infections and the practicalities of how they are managed.'* **(GP10: 33, female, 2 years)**

*'I believe in the rule of thirds. I believe a third of the patients will just get the drugs and start them anyway; a third of the patients will get the drugs and put them in a cupboard and think about starting them; and I think a third of them actually won't take them at all.'* **(GP13: 45, male, 18 years)**

*'I think just the experience of having worked for longer as a GP, just having that under your belt, I'd say.'* **(GP15: 33, female, 3.5 years)**

*'I know more about the infection and antibiotics, but that's my personal view because this is my subject of study.'* **(GP17: 67, male, 14 years)**

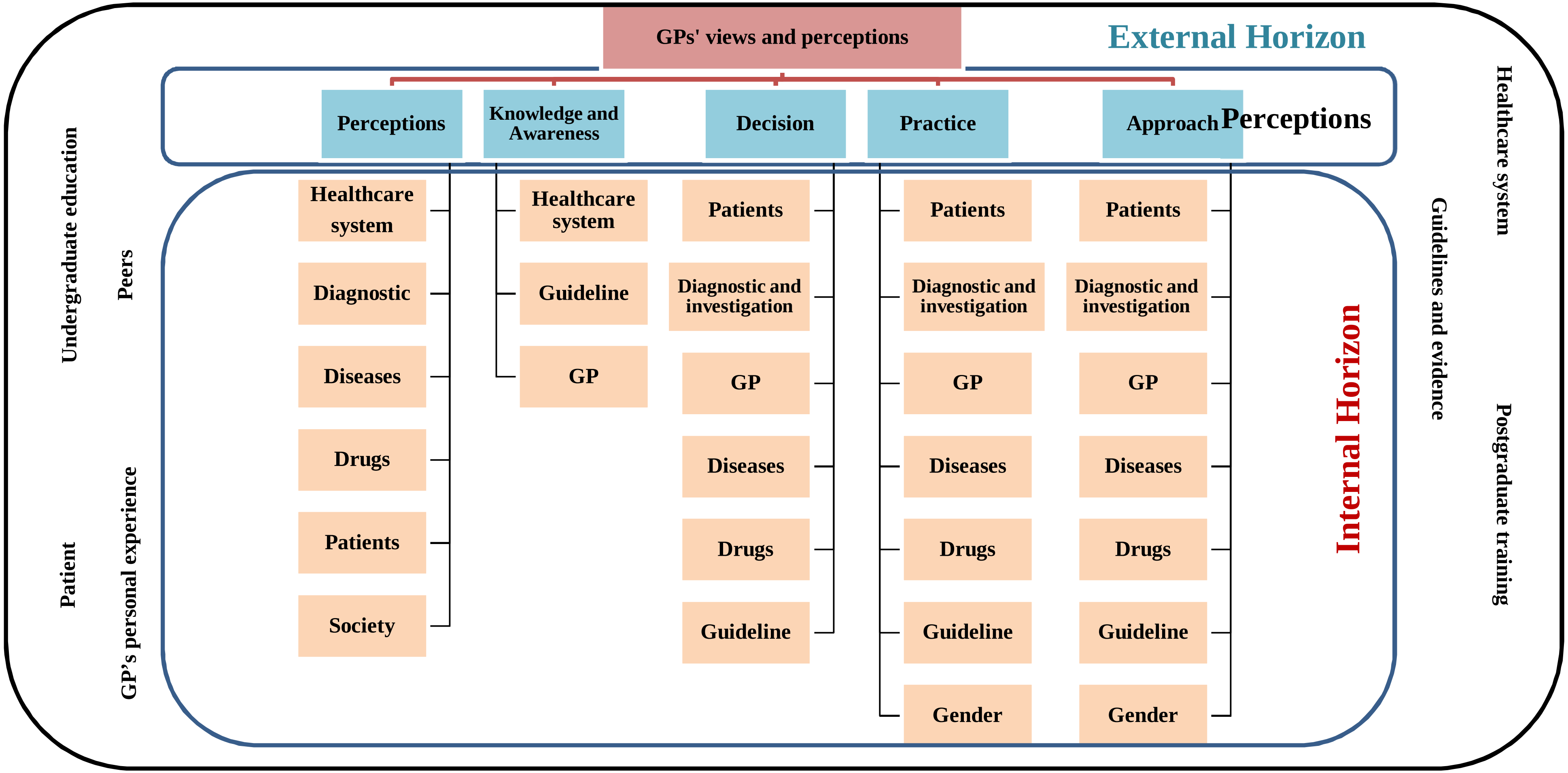



Figure 30: Summary of the internal and external horizons revealed by the GPs' interviews from phenomenographic analysis

### 5.1.5 Outcome Space

The outcome space presented here describes antibiotic prescribing practice for elderly patients with UTIs as it is experienced by GPs in GP surgeries. The categories have been arranged on a four level hierarchical block ranging from simple to more sophisticated category as illustrated in Figure 31. Knowledge was placed on level one because it is the least complex way of viewing antibiotics in elderly patients with UTIs as a result of interaction within the healthcare system itself, GPs and guidelines. In level two, the decision category was placed above knowledge owing to the more complex interaction with the internal horizon. Level three was shared between the approach and practice categories because the experience of antibiotics in both was more complex than in the previous two categories. The perceptions category was placed at the top of the hierarchy on level four owing to the complexity of the interaction between the category components and incorporating the wider context of all previously highlighted internal horizons such as national healthcare system and society.

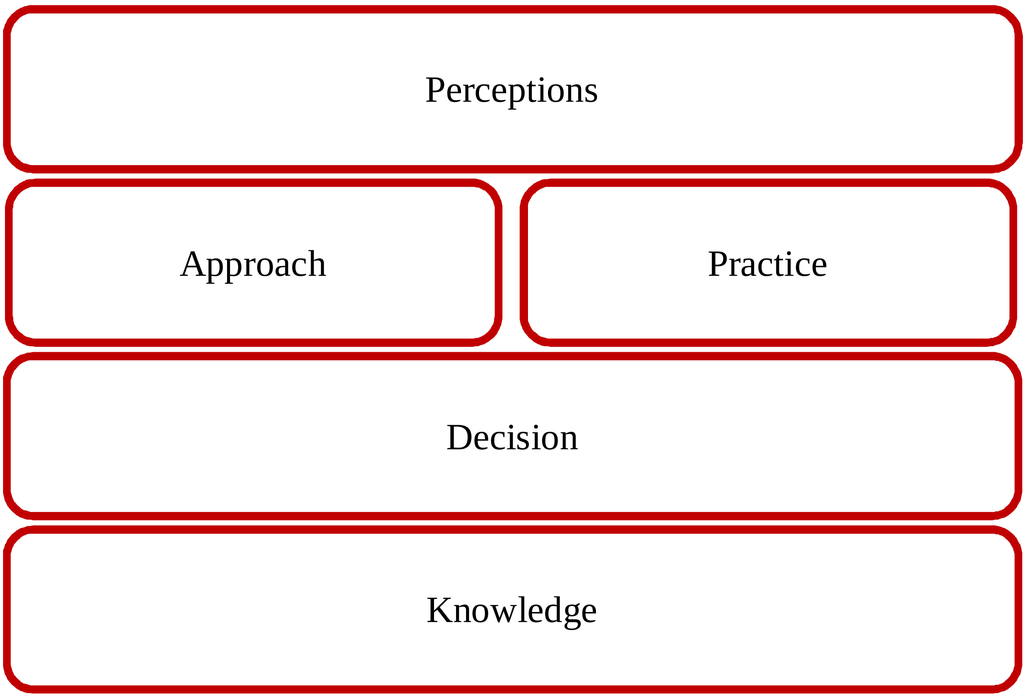



Figure 31: Four-level hierarchical representation of categories of description for antibiotics prescribing by GPs

## 5.2 Discussion about Phenomenographic Analysis of the Variations in GPs' Views on and Perceptions of Prescribing Antibiotics for Elderly Patients with UTIs

The application of phenomenographic, semi-structured interviews with phenomenographic analysis was successful in identifying the diversity and complexity of GPs' perceptions of and views on antibiotics prescribing for elderly patients with UTIs. This variation could make antibiotics prescribing deviate in key principals from rational GP decision-making as a result of GPs themselves, clinical, economic, regulatory and social factors. This may explain why interventions do not tend to be effective, as shown by a quantitative systematic review of 46 cases aimed at identifying the factors, attitudes and knowledge linked to misprescription of antibiotics (Lopez-Vazquez *et al.* 2012). Capturing all of the GPs' shared and conflicting perceptions and views in their natural context was difficult as these perceptions and views were usually *'visible'* only within each elderly patient consultation. The attempt to capture the GPs' perceptions and views was further limited by the fact that no individual can ever be certain of what is going on in someone else's mind. This section discusses these perceptions and views in relation to the literature reviewed earlier in Chapter Two.

### 5.2.1 Categories of Description GPs' Views and Perceptions

Phenomenographic analysis of the data suggested that GPs' views on antibiotics for elderly patients with UTIs fitted into five qualitatively distinct categories: perceptions, knowledge, decision, practice and approach. The first category of description showed variations in the way the GPs perceived antibiotics as a group of drugs. The inductive nature of phenomenographic data analysis identified six dimensions of variation within this category. The majority of GPs interviewed (N = 15) admired and appreciated antibiotics as a group of drugs. Within this dimension, GPs elaborated extensively on the therapeutic values of antibiotics, considering them one of the greatest innovations of the last century as well as being capable of saving thousands of patients' lives if used appropriately to treat bacterial infections (Powers 2004). However, having appreciation for and trust in antibiotics' efficacy and value does not give GPs the right to over-prescribe them without clear evidence or to prescribe them inappropriately. This was the view of another group of GPs (N = 3) who pointed out the essential role of antibiotics in practising medicine and treating infectious diseases, in line with the findings of Duane *et* *al.* (2016) who acknowledged GPs' knowledge about AMR and highlighted the value of antibiotics as part of modern healthcare while stating that they should not be over-prescibed, to avoid the long-term negative consequences for society (Duane *et al.* 2016). This perception was highlighted mainly by GPs whose main intention was to treat patients for bacterial infections and save their lives. A similar perception was reported in several qualitative studies such as Bjornsdottir and Hansen (2002) and Bjorkman *et al.* (2011), who indicated that GPs valued the efficacy of antibiotics and indicated that they should be protected for future use through restrictive antibiotics prescribing. Although this might be inconvenient, it is something GPs and patients need to get used to. Patients must be instructed about their symptoms and advised to get back to GPs only if the symptoms worsen as reported by GPs from (Bjorkman *et al.* 2011) study.

A second dimension stated by some GPs (N = 4) related to the influence of patients and public perceptions. This dimension was discussed by GPs from different viewpoints, including patients having expectations, making demands, believing misconceptions about antibiotics' microbial activity, seeing antibiotics as a cure for any type of infection and anticipating an antibiotics prescription by the end of the consultation. Having the perception that patients demand antibiotics might lead GPs to falsely assume that their patients expect an antibiotics prescription by the end of the consultation as it was indicated by a number of qualitative studies by (Petursson 2005, Kotwani *et al.* 2010, Vazquez-Lago *et al.* 2012, Bjorkman *et al.* 2013, Teixeira Rodrigues *et al.* 2013) who all highlighted GPs' misinterpretation of presumed patients' expectations without asking them about their wishes. GPs might feel that not prescribing antibiotics will damage their relationship with their patients or dissatisfy their patients. Also, they might prescribe to avoid conflict or confrontation with patients when patients just need reassurance. Therefore, GPs should first explore their patients' expectations about antibiotics in order to enhance shared decision-making, respect autonomy and to rationalise antibiotics prescribing, particularly when the patients' presentation does not warrant prescribing of antibiotics (Bjornsdottir and Hansen 2002, Petursson 2005). That said, these steps may not always be warranted owing to factors such as workload and time pressures (Petursson 2005, BMA 2014). Several studies have supported the influence of GPs' perception of patients' demands and expectations on prescribing practice (Bjornsdottir and Hansen 2002, Petursson 2005) or described it as complacency (Lopez-Vazquez *et al.* 2012, Vazquez-Lago *et al.* 2012, Teixeira Rodrigues *et al.* 2013).

A third dimension concerned perception, which GPs (N = 14) discussed in worried tones from different perspectives including patient safety, microbial resistance, loss of effectiveness and cautious use of antibiotics, mainly as a result of inappropriate prescribing, which suggests a high level of awareness about the negative consequences of antibiotics use. GPs felt that they prescribed antibiotics more wisely when they were aware of the negative consequences of inappropriate prescribing, such as side effects, future consultations and bacterial resistance. Bjorkman *et al.* (2013) and Duane *et al.* (2016) highlighted the positive influence of having a perception focused on side effects, AMR and loss of effectiveness. Furthermore, Bjorkman *et al.* (2013) considered side effects to be a factor that can cause GPs to repeat prescribe antibiotics they know are safe. However, similar concerns were considered to be influential factors in discouraging GPs from prescribing antibiotics (Petursson 2005, Kotwani *et al.* 2010, Vazquez-Lago *et al.* 2012, Bjorkman *et al.* 2013, Teixeira Rodrigues *et al.* 2013).

The fourth dimension within this category dealt with conservative prescribing practice, with a few GPs (N = 3) stating that they preferred to encourage the use of OTC drugs or non-pharmacological choices as alternatives to antibiotics before deciding to prescribe one; or that they refused to issue antibiotics prescriptions without clear evidence or indications, mainly because of their personal experience and awareness of the negative consequences of antibiotics prescribing. This perception was highlighted by Bjorkman *et al.* (2013), who linked this behaviour with GPs' level of understanding of resistance. However, GPs with this perception might not be the best GPs to consult for patients seeking antibiotics, which in turn may influence the GP–patient relationship and create a sense of patient dissatisfaction, making GPs less popular, as reported in this study and by Ashworth *et al.* (2016), who conducted a retrospective cross-sectional study in England to determine the relationship between antibiotics prescribing in general practice and reported patient satisfaction. From data from 7,800 practices, the study found that patients were less satisfied in practices that promoted prudent antibiotics prescribing. Therefore, a cautious approach to antibiotics prescribing may require a trade-off in terms of patient satisfaction (Ashworth *et al.* 2016).

A fifth dimension (N = 3) centred on the influence of guidelines that are generally meant to help GPs in terms of things like peer discussions, providing patients with explanations and making prescribing, choice and duration decisions. The GPs in this study described the positive side of using guidelines that may enhance the level of practice, as did a number of GPs in Bjorkman *et al.* (2013), who found that GPs admired the value of guidelines when it comes to prescribing. This was a common perception among GPs who considered resistance a serious threat. Additionally, another group of GPs within the same study were aware of the value of guidelines and their positive impact on prescribing and they believed that their practice must be changed towards more guideline-style prescribing. However, the influence of guidelines on GPs is still doubtful as found by one systematic review that identified seven studies out of 12 supporting the influence of guidelines on GPs' antibiotics prescribing (Teixeira Rodrigues *et al.* 2013). This inconclusive result was owing to incorporating two studies from settings other than general practice.

The last dimension to emerge from this category focused on the economic view of GPs (N = 3) who approached antibiotics as inexpensive drugs. Having such a perception might trigger GPs to prescribe antibiotics as a matter of course as seen in Bjorkman *et al.* (2013), who found that cost can influence GPs' decision to prescribe and choice of antibiotic, which might consequently increase patient demand for antibiotics in the future. Moreover, the cost of antibiotics can influence the habit of using a specific antibiotic as it becomes part of GPs' perception with time. However, economic values must not be prioritised over the cost resulting from the negative consequences of over-prescribing antibiotics, such as resistance (Petursson 2005). The influence of this perception on GPs in the UK seems to be minimal since GPs in the UK use the local prescribing formulary issued by the local CCG to assist and control GPs' prescribing decisions and cost (Knowles and Bliss 2014).

In the second category, marked variations were recognised in GPs' views in relation to their knowledge and awareness of available guidelines for UTIs in elderly patients. Three unique dimensions emerged from the data analysis. The first concerned uncertainty about the availability of any recommendations for this particular condition in that particular population. GPs (N = 6) with this view demonstrated shy or surprised reflexes during the interviews. The second dimension involved GPs (N = 8) who demonstrated a complete lack of knowledge about any recommendations. Although those GPs tried to justify and defend their position, though without really explaining the reasons for their ignorance, they were curious to know whether any guidelines existed. The final dimension within this category was affirmative awareness of specific guidelines, expressed by GPs (N = 3) who referred either to NICE guidelines or to community guidelines prepared in collaboration with NICE when they answered the question. Although the GPs in the third dimension seemed to be confident and comfortable in their answers, there were discrepancies and variations in providing details about the source and nature of these recommendations, ranging from their being part of the NICE guidelines to their being more specific and tailored to elderly patients with UTIs. Although the intention of this question was not to embarrass the GPs or evaluate their competencies, the responses reflected widespread variations across the three dimensions with regard to awareness of guidelines that might affect the quality and equity of antibiotics prescribing in terms of patient safety, trust in evidence-based guidelines and cost control (Ingemansson *et al.* 2014).

In the first two dimensions, some GPs in this study did not take responsibility for their lack of knowledge about the recommendations, preferring instead to blame guidelines publishers such as healthcare authorities and secondary care organisations for not issuing tailored recommendations for elderly patients or for not distinguishing clearly which recommendations apply to all adults and which specifically to elderly patients. This is probably true to some extent, as addressed by a number of GPs in one meta-synthesis by Carlsen *et al.* (2007) aimed at exploring and synthesising qualitative research on GPs' attitudes to and experiences with guidelines. Based on 12 studies it found that GPs claim some reasons for not following guidelines more often than others (Carlsen *et al.* 2007). This finding supports Cabana *et al.* (1999) who reviewed 76 studies to identify barriers that might prevent physicians from adhering to guidelines. This review revealed that lack of awareness and lack of familiarity were among the factors responsible for non-adherence behaviour among physicians (Cabana *et al.* 1999). Additionally, some GPs have reported lack of awareness about recommendations with regard to UTI treatment (Kuehlein *et al.* 2011). Although Bjorkman *et al.* (2013) reported on perceptions related to guidelines, the GPs in that study did not agree with the guidelines owing to the questionable efficacy of short courses of antibiotics for UTI treatment, as also highlighted by Cabana *et al.* (1999). The findings from all these studies suggest that strategies to improve GPs' familiarity with and awareness of guidelines must be incorporated into any intervention to promote prudent antibiotics prescribing.

Moreover, the GPs interviewed were interested in knowing whether any specific recommendations for UTIs existed, which might suggest a problem with guidelines dissemination and promotion. This was in line with the results from a UK questionnaire-based study of 391 GPs who considered dissemination of guidelines as one of the barriers that can influence their uptake and implementation of guidelines (Watkins *et al.* 1999). This finding was also supported by Cabana *et al.* (1999) who addressed the dissemination issue as one of the barriers that can prevent physicians from adherence to guidelines. Moreover, the findings of this category might explain and support the results from the DUR study with regard to some GPs' non-adherence to good practice points.

The third category of description successfully captured three distinct variations in GPs' perceptions associated with the process of making the decision to treat elderly patients with UTIs, which starts from the moment the GP begins to interact with the patient in the surgery. The first dimension related to elderly patients' social and medical status and was considered by all the GPs (N = 17), which might suggest the importance of this perception. Aspects discussed included patients' living status, the presence of a carer, the current clinical presentation, previous UTI episodes, UTI recurrence and co-morbidities. GPs focused heavily on patients' signs and symptoms compared with other aspects within this dimension. This combination of clinical and non-clinical factors suggests the complexity of the decision-making process, which was found to be consistent with the findings of Duane *et al.* (2016) in relation to a group of GPs who decided to treat UTI patients with antibiotics. The GPs in this group considered factors such as symptoms severity, personal circumstances, GP's and patient's previous experiences, and GP's general attitude, which can require good background knowledge and systematic evaluation, especially with elderly patients with atypical disease presentations (Beveridge *et al.* 2011). Studies of factors influencing GPs' antibiotics prescribing for infections demonstrated the importance of patients' signs and symptoms, which were described as a major and direct determinant of the decision to treat patients with antibiotics as highlighted by Petursson (2005) and Teixeira Rodrigues *et al.* (2013). Surprisingly, none of the qualitative studies on GPs' perceptions discussed these views in the elderly population and no previously published literature highlights living status as a factor in GPs' perceptions, so this can be considered a novel finding.

Diagnostic tests were the subject of the second dimension, discussed by several GPs (N = 9) as influencing the decision to treat. GPs indicated that they requested MSU most of the time owing to the fact that elderly patients with infections usually presented with atypical symptoms (Beveridge *et al.* 2011). GPs were less likely to depend on dipstick testing owing to its weak reliability when diagnosing UTIs, particularly in elderly patients, as highlighted by UTI guidelines for adults in the UK (SIGN 2012). This perception explains how GPs overcome diagnostic uncertainty about clinical presentations in elderly patients and also suggests good adherence to diagnostic recommendations. The finding from this study was in agreement with Duane *et al.* (2016) who highlighted the use of diagnostic tests by Irish GPs, specifically, dipstick testing to guide antibiotics prescribing to overcome diagnostic uncertainty. They also described a group of GPs in Ireland as *'questioning prescribers'* who believe that there is a grey zone in the diagnosis of UTIs and are more willing to question the need for an antibiotic depending on the symptoms presented to them by the patient and the dipstick results. Moreover, this group of GPs were found to be willing to change this hesitant behaviour once their antibiotics prescribing linked to AMR. In fact, the literature confirms that the use of diagnostic tests for UTIs can make antibiotics treatment more effective, reduce unnecessary antibiotics use and differentiate UTIs from ASB, which usually requires no treatment, as was supported by a systematic review of 9 cases aimed at determining the value of diagnostic testing (Schmiemann *et al.* 2010).

The third dimension related to drug safety and compliance concerns. Some GPs (N = 4) felt comfortable prescribing certain antibiotics according to their knowledge and practice experience as reported by Teixeira Rodrigues *et al.* (2013). GPs should be aware of their limitations as well as their skills to ensure that they are not prescribing beyond their knowledge and that patients are safe, as highlighted by the general practice prescribing guidelines issued by the BMA clinical practitioners committee (BMA 2013). The decision to treat can be challenging in some circumstances, especially with elderly patients who usually present with polypharmacy and co-morbidities (Bellmann-Weiler and Weiss 2009). GPs' perceptions about patient compliance with proposed antibiotic regimens can play a role in reducing inappropriate use of antibiotics. However, this might be seen as non-adherence to guidelines by some. It seems that GPs who have drug safety perceptions have greater knowledge of antibiotics prescribing issues about side effect and therefore have an attitude of explaining antibiotic side effects to their patients. However, the findings in this study about antibiotics prescribing issues and the quality of prescribing were contrary to the finding from Bjorkman *et al.* (2013) who linked the side effects perception with GPs' fear. This study was consistent with Bjornsdottir and Hansen (2002) and Kotwani *et al.* (2010) with regard to patient compliance as a determinant for antibiotics prescribing whereas in Vazquez-Lago *et al.* (2012) patient compliance was linked with AMR. Additionally, side effects were highlighted only by Bjornsdottir and Hansen (2002) as a factor that can influence antibiotics prescribing.

The fourth category of description highlighted variations in GPs' antibiotics prescribing as an essential part of UTI management. Mapping this view resulted in identifying six different dimensions. In the first dimension, several GPs (N = 6) perceived antibiotics prescribing in elderly patients in a similar way to adults. They did not make any distinction between older patients with possible co-morbidities, polypharmacy and limited reserve capacity and younger or middle-aged patients when prescribing antibiotics, whether they focused on decision, choice, dose or duration. The finding from this category was inconsistent with the findings from one qualitative grounded theory interview study of 40 GPs from the UK, aimed at exploring GPs' reasons for prescribing antibiotics for general infections, and found that being elderly is one of the reasons for prescribing antibiotics in a different way from other age groups (Wood *et al.* 2007). This dimension emerged from GPs with long years of clinical practice experience who stated that they practise mainly based on their clinical experience, although no experience can be a substitute for evidence-based guidelines as reported in a qualitative focus group study aimed at identifying the barriers to the implementation of UTI guidelines as perceived by 13 GPs from the Netherlands and exploring interventions to overcome them (Lugtenberg *et al.* 2010).

On the contrary, the second dimension clearly distinguished between elderly patients and the rest of the population. GPs with this view (N = 7) described a low-threshold of prescribing, that is, more antibiotics prescribing, initiating antibiotics treatment as early as possible, and using antibiotics with altered durations compared with adult patients. However, this practice might be seen as non-adherence to guidelines if there were no specific recommendations concerning elderly patients or no clear distinguishing between elderly and other age groups. Moreover, GPs within this dimension expressed their worry and the need to be mindful, careful and cautious whenever prescribing antibiotics for elderly patients owing to multiple factors such as frailty and fear of developing further complications. This perception might favour prescribing antibiotics for elderly patients, although the GPs stated that this should not be without clear evidence of infection. GPs showing concern is a good sign as it makes them consider whether the benefits outweigh the risks before making the decision to treat. This finding was consistent with Wood *et* *al.* (2007) who tended to consider being elderly as a reason to start antibiotics very early to prevent deterioration of patient condition.

The third dimension related to elderly patients' social and medical status. In this dimension, GPs (N = 4) intended to provide elderly patients with UTIs with a better quality of care by considering their surrounding social lives, future accessibility to GP re-consultation and co-morbidities. This finding was in line with the findings from Teixeira Rodrigues *et al.* (2013) who considered the presence of a direct relationship between patients' social factors and GPs' antibiotics prescribing for the general population.

Safety and compliance concerns were the fourth dimension, seen in the form of cautious and careful prescribing practice with emphasis on drug interactions, side effects, appropriate dosing and patient compliance. GPs (N = 4) with this view reported awareness and understanding of elderly patients' special considerations as part of their practice. It seems that GPs who have drug safety and compliance perceptions have greater knowledge of antibiotics prescribing issues and therefore have an attitude of explaining antibiotic side effects to their patients.

The fifth dimension, centred on adhering to and implementing local guidelines, was reported by a few GPs (N = 3) who took a firm position on adhering to guidelines, whether local, national, diagnostic or treatment, to avoid any mistakes in prescribing for this vulnerable population. No previous work has been done to determine the perception of GPs with regards to antibiotics local recommendations. However, the finding from this study was in line with Teixeira Rodrigues *et al.* (2013), who considered implementing policies and guidelines as a factor that might contribute to GPs' antibiotics prescribing for the general population.

The last dimension involved the use of diagnostic tests, mainly in the form of MSU to confirm UTIs, to justify antibiotics prescribing. A few GPs (N = 3) who reported this perception admired the value of diagnostic tests in elderly patients especially if the patient examination showed atypical presentation for UTIs, which is the main case with elderly patients (Beveridge *et al.* 2011). GPs expressed feeling comfortable whenever they based their antibiotics prescribing on MSU results as this practice is associated with prudent antibiotics prescribing and provides GPs with confidence, especially when there is a chance for diagnostic uncertainty. This was in agreement with the findings from Duane *et al.* (2016), who explored Irish GPs' use of diagnostic tests, specifically, dipstick testing, but not MSU to guide antibiotics prescribing especially when there was a grey zone in the diagnosis of UTI.

Overall, this category showed different perceptions and views that either oppose other views, as is evident in dimensions one and two, or have different perspectives on existing views. This might explain the widespread variations in antibiotics prescribing that were quantified and identified in the DUR study. The findings also suggest that some GPs can have a high level of awareness of the value of diagnostic tests in elderly patients with UTIs, especially if patients present with atypical symptoms, and of distinguishing UTIs from ASB. They also suggest that some GPs are aware of aspects of prescribing practice for elderly patients, especially safety and compliance.

No previous work has been carried out to explore GPs' perception in terms of antibiotics prescribing approach for UTIs in the elderly population. Searching the literature resulted in identifying two qualitative works that contain a little information on antibiotics prescribing for elderly patients in general. One was excluded as it discussed antibiotics for elderly institutionalised patients with ASB. The included study was carried out in 1995 and focused on 10 Icelandic GPs using qualitative, in-depth interviews to understand the use of evidence by GPs in the diagnostic process preceding antibiotics prescribing in the general population (Bjornsdottir *et al.* 2010). The only finding relevant to this research and in agreement with the research findings was that physicians tend to prescribe antibiotics for elderly patients on the *'slightest suspicion'* of all infections except for sinusitis. The GPs in this study also used the term *'low-threshold'*.

The fifth and final category of description in this study deals with variations in antibiotics prescribing for elderly patients with UTIs based on gender. GPs in this category showed two different dimensions. The first dimension supports the concept of approaching elderly male patients in a different way, whereas the second dimension supports treating elderly male and female patients the same as other adults. GPs (N = 10) within the first dimension highlighted taking a more aggressive approach to treating male patients, either by choosing broader-spectrum antibiotics or by prescribing for extended durations without indicating the reason for such practice, whereas the rest of the GPs explained that males tend to have prostatitis and get more complicated infections than females. Using broader-spectrum antibiotics, alternative antibiotic choices or longer therapy durations without clear justification might be a strong indicator of inappropriate antibiotics prescribing and non-adherence to recommendations when treating this vulnerable group of patients. GPs (N = 7) with the second view did not consider gender to be a factor in the process of prescribing antibiotics for elderly patients with UTIs. Although those GPs acknowledged the presence of certain differences between genders with regard to process and aetiology, they did not consider these to be determinants for treating differently. As in the previous category, no previous qualitative work has been carried out to explore variations in GPs' antibiotics approach for different sexes. From a quantitative perspective, studies on adherence to antibiotics guidelines demonstrated this variation in GPs' prescribing according to patient sex. For instance, Haasum *et al.* (2013) found that 1,457 (32.1%) elderly females received pivmecillinam whereas 1,584 (68.2%) males from the same age group received quinolones. Another study by Leistevuo *et al.* (1997) revealed variations in prescribing between male and female elderly patients as 36% (N = 50) of elderly male patients received first-generation cephalosporins whereas 37% (N = 94) of elderly female patients received TMP-SMX or trimethoprim. In both studies, the link to guidelines, diagnoses and culture and sensitivity results needs to be explored before stating whether this variation is because of gender differences or other factors such as UTI type and susceptibility of infecting pathogen.

Although there were several variations noticed during this study, several dimensions were found to be similar across the different categories, including patients' socio-medical status, antibiotics concerns, diagnostic tests, patients' safety and compliance, and the no variation dimension between elderly and adult patients or between elderly male and elderly female patients. While these dimensions seem to be similar at first glance, however, the perspectives of participants likely differed according to the nature of the specific question, their experience and perspective. For instance, diagnostic tests were discussed in category three as a tool for guiding diagnosis whereas in category four they were discussed as a tool for guiding antibiotic therapy. This finding can be helpful in terms of designing a comprehensive intervention that incorporates all GPs' perspectives.

### 5.2.2 Outcome Space and Internal Horizon

From the outcome space perspective (Figure 31), knowledge and awareness of available guidelines have the least complex relationship with GPs' antibiotics prescribing for elderly patients with UTIs. The healthcare system and guidelines were the central focus of GPs' knowledge and awareness. On the second level, the decision to treat was seen to be more complex than knowledge as it focused on patients, diagnostic testing and investigation, GPs, diseases, drugs and guidelines. Practice was placed on the third level of the hierarchically ascending outcome space diagram, alongside approach. In these two categories, the relationship between approach and practice compared with other categories was found to have commonalities with the components of both decision and knowledge. The process of prescribing an antibiotic requires GPs to be knowledgeable about and familiar with diseases, patients, gender variations, guidelines, diagnostic testing and investigation, and drugs. Perceptions were located at the top of the hierarchical structure as they represent the most complicated GP views on antibiotics prescribing for elderly patients with UTIs. In addition to including the components from the other categories, perceptions concern how antibiotics prescribing affects society as a whole as well as the economic aspects of antibiotics. Only one phenomenographic study was identified from the reviewed literature with regard to UTIs. However, this study did not present, interpret or discuss the outcome space and internal horizon (Bjorkman *et al.* 2013).

### 5.2.3 External Horizons

The analysis revealed seven external horizons that helped to shape GPs' understanding and practice of antibiotics prescribing. These horizons were undergraduate education, postgraduate training, personal experience, interaction with peers, interaction and influence of patients' expectations, the healthcare system, and availability of guidelines and evidence.

GPs' undergraduate education and postgraduate training can be considered part of their core experience and knowledge of antibiotics prescribing as shown by a Canadian historical cohort study of 852 primary care physicians to assess whether physician knowledge, time in practice, place of training and practice volume explain the differences in antibiotics prescribing among physicians and linking inappropriate antibiotics prescribing with physicians who received their training and education abroad, which might be related to cultural expectations (Cadieux *et al.* 2007). University education was also identified as one of the factors that can influence GPs antibiotics prescribing as reported by (Teixeira Rodrigues *et al.* 2013). During undergraduate study, GPs usually come across antibiotics and elderly patients for the first time, through pharmacology and pharmacotherapy courses that provide them with basic knowledge of these drugs and this population. However, it was found that little curricular time was devoted to elderly patients' pharmacology and that educational programmes have not been thoroughly evaluated, as reported by one systematic review aimed at exploring the quantity and nature of geriatric pharmacology education in undergraduate (12 hours) and postgraduate curricula for GPs (11 hours) including the UK (Keijsers *et al.* 2012). In their postgraduate training, GPs are exposed to a variety of antibiotics for treating different infectious diseases, and involved in the process of medical decision-making, including prescribing and managing real cases under the supervision of specialised consultants (Kuehlein *et al.* 2011). During the interviews, some GPs did mention the influence of postgraduate training on their antibiotics prescribing practice and perceptions, although, as time went on, they became more confident in addition to being influenced by their practice environment. Kuehlein *et al.* (2011) described the influence of postgraduate hospital training as a key factor in the development of GPs' prescribing behaviour supported this horizon from the research. GPs' postgraduate education and training also play a vital role as these two factors were linked with the quality of prescribing in different studies (Akici *et al.* 2004, Kamarudin *et al.* 2013) as a result of their abilities to maximise GPs' knowledge, keep GPs updated, reduce prescribing errors and impact the quality of care delivered to patients. Targeting clinicians early, at the point of education and training, can have a great impact on their antibiotics prescribing behaviour, as suggested by one qualitative study of 80 GPs from nine European countries about antibiotics prescribing decisions for LRTIs (Brookes-Howell *et al.* 2012).

Another horizon identified by the analysis was GPs' personal experience, which evolves through GPs' continual prescribing and exposure to different cases. In practice, GPs prescribe antibiotics from a range they are familiar with. This habitual experience and skill is usually gained over years of practice as a GP, sharpening the knowledge they gained during undergraduate education and postgraduate training. In this study, the GPs had different years of practising experience, during which they came into contact with countless elderly patients with UTIs whom they managed with different antibiotics. GPs reported experience as being one of the factors that shape their antibiotics prescribing in two qualitative studies of UTIs (Kuehlein *et al.* 2011, Duane *et al.* 2016), both of which reported that previous experience can reinforce the norms and expectations of their practice particularity for antibiotics therapy, which also supports the findings from this study.

Interaction with peers was found to be another external horizon that affects GPs' antibiotics prescribing. Whether the interaction is formal or informal, GPs share, communicate and discuss many things such as knowledge, experience and advice. GPs might consult their peers, who might be working with them within the same surgery, or in the local hospital, microbiology laboratory or academia, to seek advice about a diagnosis or an antibiotic for a specific patient's condition. This interaction might result in the iterative development of prescribing habits, which in turn might develop into a perception. This factor was highlighted by GPs in one qualitative research (Kuehlein *et al.* 2011) in relation to antibiotics prescribing for UTIs. The findings from that research named peers and interaction with peers as one of the strongest influences on GPs' treatment decisions perception.

Patients were also seen as major determinants of GPs' antibiotics perception development. Patients may interact and influence GPs' perceptions in different ways such as through their expectations and by exerting pressure. For instance, patients might visit their GP expecting an antibiotic, or GPs might assume that is the case when the patients are only looking for reassurance (Duane *et al.* 2016). In some cases, patients might start demanding antibiotics without a clear indication or push GPs towards particular antibiotics even if they are inappropriate for their condition. Consequently, GPs might prescribe antibiotics unnecessarily or inappropriately in both situations. This practice has been described in much qualitative literature using different terms including complacency (Vazquez-Lago *et al.* 2012, Teixeira Rodrigues *et al.* 2013). In line with this research finding, both Bjorkman *et al.* 2013 and Duane *et al.* (2016) identified the same perception with GPs who were aware of both patients expecting antibiotics and patients seeking reassurance. Additionally, GPs from Duane *et al.* (2016) study stated that it is much more difficult not to prescribe for patients visiting private clinics because they are paying for what they are getting.

The healthcare system was identified as a major contributor to GPs' views and perceptions. GPs referred to topics relevant to the healthcare system to describe its influence over antibiotics perceptions, including resource constraints, scheme incentives, guidelines and policies, and patient access to antibiotics through out-of-hours services. The healthcare system context can shape GPs' perceptions through their immediate environment – the GP surgery – on a CCG level or through a national context as discussed by research focused on the quality of GP prescribing in England under the influence of current challenges (Duerden *et al.* 2011). Limited surgery budgets, low salaries, increased working hours and very strict policies can all restrict GPs' decisions and options (Taylor *et al.* 2012, BMA 2014). For instance, the influence of time pressure can be seen clearly in situations where demanding patients insist on getting antibiotics. The standard consultation length according to policy is 10 minutes while the actual average length spent with patients ranges from 10 to 15 minutes (Lakhani *et al.* 2007) and there is usually a queue of patients waiting. All this can force GPs to prescribe unnecessary antibiotics just to put an end to consultations with demanding patients. This influence of the healthcare system on GPs' external horizon has been reported by several other qualitative studies (Petursson 2005, Vazquez-Lago *et al.* 2012, Teixeira Rodrigues *et al.* 2013) as one of the non-pharmacological behavioural determinants of GPs' antibiotics prescribing for general infections.

Guidelines and evidence were highlighted by the interviewed GPs as another external horizon responsible for shaping their antibiotics prescribing practice. Although guidelines and evidence might be considered a cornerstone of medical practice, some GPs do not always adhere to them either because they depend on their practice experience or because they believe they are not in the best interests of their patients. This is similar to the findings from one meta-synthesis that explored GPs' attitudes to and experiences with guidelines (Carlsen *et al.* 2007). However, guidelines could be one of the best ways of rationalising practice and replacing the idiosyncrasies of individualised decisions, that is, standardising practice (Watine *et al.* 2014). There were discrepancies in GPs' awareness of recommendations in this study. However, several GPs valued the guidelines when diagnosing and prescribing antibiotics, especially in cases where uncertainties are present or when dealing with elderly patients, who are particularly vulnerable. The influence of guidelines has been discussed inconclusively in many qualitative studies as a result of including studies from non-primary care settings such as surgical wards and emergency departments (Teixeira Rodrigues *et al.* 2013). However, the finding about guidelines and evidence as an external horizon for GPs' antibiotics prescribing in this study is in line with Kuehlein *et al.* (2011), who noticed an improvement in GPs' prescribing practice and acceptance of guidelines after a focus group discussion about guidelines and current GPs' prescribing attitudes. Bjorkman *et al.* (2013) found that GPs who prescribe antibiotics rationally are those influenced by and compliant with UTI guidelines. Additionally, Duane *et al.* (2016) reported that GPs were aware and influenced by UTI guidelines but rarely cited them as the primary reason for antibiotic treatment decisions.

Given the fact that this was one of the first studies to capture and map GPs' perceptions of antibiotics prescribing for elderly patients with UTIs in the UK, several findings were considered to be novel, adding to what is already known, while others were comparable with the previously reviewed literature in Chapter Two. The findings relating to training, education and interaction with peers were in line with Kuehlein *et al.* (2011), who identified peer group interaction, personal experience and previous medical training as the main drivers behind German GPs' prescribing behaviour, leading to reflex-like treatment decisions. Additionally, the influence of guidelines and evidence in shaping GPs' prescribing attitudes and rationalising prescribing was in agreement with the findings from (Kuehlein *et al.* 2011, Bjorkman *et al.* 2013, Duane *et al.* 2016). Looking at the study by Duane *et al.* (2016), GPs in the UK shared perceptions with GPs from Ireland in relation to antibiotics prescribing, society, diagnosis and treatment of UTIs, which were considered to be easy to diagnose and treat. Social and medical factors were shown in this study to influence GPs' decision to prescribe. Although the interpretation may be different owing to differences in the method of analysis, the perceptions are there. From a treatment perspective, in both studies GPs reported that treatment usually started empirically as a result of the delay between sending the sample off for testing and obtaining the microbiological results to confirm UTI. Moreover, the influence of GPs' attitudes, socio-demographic status, knowledge, patient-related factors, CCG and healthcare system for driving antibiotics prescribing by GPs was clearly documented in this study, which is consistent with the findings from (Bjornsdottir and Hansen 2002, Petursson 2005, Kotwani *et al.* 2010, Vazquez-Lago *et al.* 2012, Teixeira Rodrigues *et al.* 2013).

Side effects, concerns and compliance were discussed in this study in terms of understanding, elderly patients and the quality of prescribing, whereas Bjorkman *et al.* (2013) discussed them from a fear perspective. GPs discussed the influence of guidelines from a positive standpoint, unlike the GPs from Bjorkman *et al.* (2013) study who were both positive and negative. Moreover, GPs in this study showed a lack of familiarity and awareness with regards to UTI guidelines, which is not the case for the GPs in Bjorkman *et al.* (2013), who referred to lack of agreement as a reason for not following UTI guidelines. Another key difference from other studies is that in this study GPs valued the use of diagnostic tests in guiding antibiotics prescribing, particularly MSU but not dipstick resting as highlighted by Duane *et al.* (2016), which could be owing to differences in diagnostic guidelines between the two countries. Additionally, uncertainty was present in Duane *et al.* (2016) study in relation to diagnosis and prescribing whereas in this study uncertainty was seen as a perception related to knowledge and awareness of UTI guidelines.

### 5.2.4 Future Research

The findings from this study suggest the presence of variations in GPs' views and perceptions, often within the same category. Additionally, variations in knowledge of guidelines might be responsible for GPs' non-adherence. Some GPs reported contrasting views about how elderly patients should be managed compared with adult patients, as well as how elderly male patients should be treated compared with elderly female patients. Therefore, it would be interesting to know the factors that may influence GPs' prescribing decisions for adults and elderly patients with UTIs. Future thematic analysis should be carried out to identify these factors in the two age groups.

## 5.3 Findings from Thematic Analysis of Various Factors Influencing GPs' Prescribing of Antibiotics for UTIs

The following section presents the findings that emerged from the thematic analysis of the interviews with regard to factors influencing GPs' prescribing of antibiotics for UTIs in elderly patients in comparison with adults. Three main categories, comprise the themes and sub-themes that emerged from the interviews analysis [31]. The analysis resulted in identifying a total of 29 factors to influence GPs antibiotics prescribing for UTIs. These can be found in Table 32. Both themes and sub-themes were consolidated into one of the three categories based on (Watt *et al.* 2007) definitions and prescribing models discussed earlier in Chapter One . During the interview, GPs were asked to highlight and discuss the different factors that might influence antibiotics prescribing for UTIs and whether there is/are differences in these factors between adult and elderly. If there were no differences between adult and elderly, the factor will be described in general however when GPs indicated presence of a difference in the factors between adult and elderly patients a comparison was made, supported by GPs' quotes.

[31] The words 'themes' and 'sub-themes' are used interchangeably with the word 'factor(s)' in this thesis.

Table 32: Themes (factors) that emerged from the thematic analysis categorised into three main categories

| Category | **Definition** (Watt *et al*. 2007, p. 29) | Themes (factors) |
|---|---|---|
| **Micro-level** | Factors related to individual GP and patient interaction context | ***Intrinsic factors*:**<br>**GPs' sociodemographic**<br>▪ GPs' personal experience and familiarity with specific antibiotics<br>▪ GPs' education, knowledge and training<br>**GP attitude**<br>▪ Complacency<br>▪ Fear<br>▪ Responsibility of other HCPs<br>**Others**<br>▪ Antibiotic resistance threat, microbial resistance results and information about local resistance pattern<br>▪ GPs' antibiotic prescribing concerns<br>▪ Diagnosis and clinical decision making<br>▪ GPs' ethos and ethical values |
| | | ***Extrinsic factors:***<br>**Patient's related factors**<br>▪ Patient's age and gender<br>▪ Patient's medical history and clinical characteristics<br>▪ Patient's social situation and living conditions<br>▪ Patient's level of understanding and knowledge<br>▪ Patient's desire for a quick fix<br>▪ Patient's autonomy |
| **Meso-level** | Factors related to practice or CCG context | ▪ Visits and education by prescribing advisors,<br>▪ Audit, monitoring and feedback of prescribing<br>▪ Influence by secondary care doctor prescribing practice<br>▪ Implementation of local policies, guidance and formulary |
| **Macro-level** | Factors related to society, national or international context | ▪ Time<br>▪ Guidelines and evidence<br>▪ Antibiotics shortage<br>▪ Incentives<br>▪ Media<br>▪ Cost<br>▪ Healthcare resources and constraints<br>▪ Pharmaceutical companies<br>▪ Over-prescribing<br>▪ Society experience and expectation |

### 5.3.1 Factors Influencing GPs' Antibiotics Prescribing for UTIs

#### 5.3.1.1 Category 1: Micro-Level Factors

In this category, factors related to GP characteristics as well as GP–patient interactions were discussed. The category can be further divided into two main themes – intrinsic factors and extrinsic factors – which between them include 15 factors.

##### *5.3.1.1.1 Theme 1: Intrinsic Factors (GP-related Factors)*

Numerous factors within this theme were highlighted and discussed by participants as influencing the way they experience antibiotics prescribing. Collectively, they were found to be part of a broader three categories that mainly related to GPs' characteristics as important factors in influencing antibiotics prescribing. These include GPs' socio-demographic profiles, GPs' attitudes and others. The following section discusses these factors in detail with the use of appropriate quotes from participants' interviews.

###### *5.3.1.1.1.1 GPs Socio-demographic*

###### *5.3.1.1.1.1.1 Personal Experience and Familiarity with Specific Antibiotics*

Looking at the socio-demographic aspects of GPs, first, in terms of GPs' personal experience and familiarity with specific antibiotics, several participants (N= 6) stated their personal experience of infectious diseases and familiarity with specific antibiotics to be one of the strongest factors that might influence and shape their antibiotics prescribing. Participants who considered this factor used the *words 'personal'*, *'familiarity'*, *'knowledge'*, *'previous'* and *'experience'* to describe it.

This quote supports participants' familiarity with antibiotics through experience as one of the factors that can influence antibiotics prescribing:

> *'I think your own familiarity with medications, that there may be that there's a couple of medications appropriate. You know the dosage. You know the side effects of one well, so I think you tend to go back to that. Just your own experience of using it.'* **(GP2: 58, male, 29 years)**

Another quote describes how the participant's judgement and habits of prescribing could be based to an extent on his personal experience with antibiotic relating to a previous patient:

> *'My judgments and habits may also be based on some of my personal experience so what will I've seen worked and not worked for certain patients.'* **(GP8: 36, male, 2 years)**

Another quote describes experience and knowledge of certain antibiotics as influential factors on prescribing:

> *'Your experience of using antibiotics. Your knowledge of certain antibiotics.'* **(GP12: 35, female, 5.5 years)**

A fourth participant explains how previous subjective experience with antibiotics can raise the level of confidence in prescribing until it becomes a habit:

> *'It's also your experience in these different medications, whether you're confident prescribing them, if you felt confident about patients who got better on them in your subjective experience, and that often will flavour which drug you use. It's kind of how you've experienced these drugs before. The psychology of it, really.'* **(GP14: 34, male, 5 years)**

***5.3.1.1.1.1.2 Education, Knowledge and Training***

GPs' undergraduate education, postgraduate training as well as Continuing Medical Education (CME) were said to be a key influencing factor in antibiotic prescribing since education is likely to be the core of GPs' experience and knowledge. Participants (N = 6) who considered this factor used utterances such as *'knowledge'* and *'training'* in the discussion.

In the following quote, the participant explained how her previous medical training and practice in an infectious diseases unit in a hospital during her internship shaped and influenced her current antibiotic prescribing owing to her exposure to different cases and her having to work in line with the standard procedures and protocols within that hospital:

> *'I think really just working in a hospital. Seeing more patients. Seeing patients with infections. And the practicalities of how they are managed. I worked in the infectious diseases unit, which I think has influenced me quite a lot, because during that time, my knowledge of using antibiotics was hugely increased knowledge of the test they do. The lab part. Getting the importance of getting samples at the beginning of an illness, rather than only if it doesn't work. Because we were seeing the patients who weren't responding to antibiotics. I think that's definitely influenced my practice in general practice.* **(GP10: 33, female, 2 years)**

Another participant said that he considers training and education to be core for his prescribing antibiotic attitude:

> *'Well, I guess your own training in medicine and what you've learned as a trainee.'* **(GP13: 45, male, 18 years)**

#### *5.3.1.1.1.2 GPs' Attitudes*

##### *5.3.1.1.1.2.1 Complacency*

This factor was considered a major driver for antibiotics prescribing and was stated by all the participants (N = 17) using different words to describe it such as *'demand'*, *'pressure'*, *'expectation'*, *'desire'*, *'previous experience'* and *'need'*.

In this quote, a GP addressed complacency as a factor affecting antibiotics prescribing. He explained why this attitude is common among GPs, for reasons that include avoiding to confront angry patients, concern about losing the GP–patient relationship and pleasing patients, although he was aware that this attitude could result in increased bacterial resistance:

> *'Every GP dreads the angry patient ... the angry patient who comes in demanding treatment. It's much easier to give it and say, 'Okay, you want antibiotics? I don't think they're going to work, but you might as well take them anyway. I can see how strongly you feel. I want you to leave happy rather than upset, so here's your antibiotics.' That, if you like, is the path of least resistance. It's too easy, sometimes, for a GP to do that; it's too easy for the GP to be a people pleaser…. Of course it will increase resistance; of course it will also increase their likelihood of coming back again and again and again. Each time they get those symptoms, they expect each time to have antibiotics… In general practice, the patient ... the individual ... is more important than the population, and an individual relationship. And yes, there may be resistance in the community, but that's a more theoretical concern. What's a more immediate concern is the individual patient in front of you. My argument would always be it's so important to see the bigger picture, that you're creating a longer-term crisis of resistance; but when you've just got one patient in front of you, that patient says, ''That crisis of resistance is nothing to do with me. I need some treatment now. I'm sick. Can't you see I'm sick?.''* **(GP2: 58, male, 29 years)**

A participant illustrated how patients can be very forceful about getting antibiotic prescriptions because they expect them:

> *'A patient's desire to have an antibiotic. Their expectation of what you are going to do for them, and if they you know how forceful they are in demanding an antibiotic will certainly influence prescribing practices, I think… Yeah. Your perception of how much they're going to kick-off if you don't prescribe.'* **(GP9: 30, female, 2 years)**

Another participant discussed how patients' expectations can be a driving factor affecting antibiotics prescribing:

> *'Patient expectation is a big one… if patients have a clear expectation that an antibiotic is what they're going to come away with from the consultation then that*

*is quite a powerful drive… I think with patients that have prior expectation is one of the main factors.'* **(GP13: 45, male, 18 years)**

This quote describes how patients' expectations can go beyond having an antibiotic; they sometimes ask for a much stronger one because they have been given it in the past regardless of its appropriateness:

*'Expectation from patients that you're going to prescribe them antibiotic. When they don't actually need it because they haven't got a bacterial infection. But then also some patients often ask for a strong antibiotic because they've been given something before, either appropriately or inappropriately.'* **(GP15: 33, female, 3.5 years)**

A few participants, mainly females, elaborated on complacency as a key factor of antibiotics prescribing when they discussed elderly patients with UTIs. A young female participant illustrated how elderly patients can be very demanding when it comes to receiving antibiotic prescriptions for UTIs:

*'They'll come and they'll be demanding antibiotics but that might well be the appropriate thing for them at that point.'* **(GP4: 33, female, less than a year)**

Yet a second participant referred to elderly patients' expectations as a factor in the kind of complacency that affects the prescribing of antibiotics:

*'I suspect with UTIs and elderly patients, there's just more of an expectation that they will get antibiotics and that they need them. If they don't have antibiotics, it's not going to go away on its own.'* **(GP12: 35, female, 5.5 years)**

One participant referred to both patients' perceptions and patients' demands to describe the complacency factor that influences prescribing antibiotics for elderly patients with UTIs:

*'Sometimes they keep on asking for antibiotics but that can also be too good to though, other reasons why they're thinking about antibiotics why they need antibiotic. So, patient perception.'* **(GP16: 42, male, 4 years)**

Additionally, elderly patients' carers, whether family members or nursing home staff, were seen as part of this factor. Carers usually expect their patients to receive antibiotics during consultations for several reasons such as fear of patients' conditions getting worse, belief that antibiotics are the drug of choice, and desire to relieve patients' symptoms and shorten the duration of the disease. This influence exerted by carers was described by a few participants as a part of complacency, as can be seen in the following quotes:

*'I think also if the patient is elderly themselves and they're vulnerable, they can't vocalise their concern, it makes the treatment they receive can very much be*

> *subject to the will of the individual doctor or the pressure by those around them whether that's the family or carer.'* **(GP3: 35, female, 5.5 years)**

> *'I think there is again pressure from carers of nursing homes to prescribe and because they often don't see the patient and they do it over phone and they ring, they might say 'oh well I'll fax a prescription and you can get it.'* **(GP5: 45, male, 9 years)**

***5.3.1.1.1.2.2 Fear***

This was described by two participants (N = 2) as one of the factors that could influence her prescribing antibiotics. She gave an example about treating an autistic child who was sick for almost four weeks. The participant linked her antibiotic prescribing for this child with the mother's previous experience and her concern about the possible deterioration of this child's condition:

> *'I had this case today. It was with a child actually so the mom … The child had a cough for four, three and a half to four weeks now and the child is 10 or 11 and has autistic spectrum disorder so the communication is not excellent there and so mom was very worried that he'd end up in hospital with a chest infection. It did happen in the past about two years ago and she was worried and this is the same pattern. It started and the cough persisted and then it's getting worse. When I examined him, I did not find any evidence of lower respiratory tract infection but ultimately I had this mom to deal with that I had to then instil confidence in her and also actually make her feel validated that she's got some quite genuine concerns. I've got a child who doesn't communicate very well particularly in him. If he's going to get sick, we'll find out a bit later than in other kids so there I gave her a prescription with the agreement that actually she would hold off at least until the weekend and see how he is after a few days.'* **(GP7: 37, female, 6 years)**

This factor was also described by one participant when she discussed the case of an elderly patient with a UTI. The female participant indicated that she might prescribe more antibiotics for elderly patients with UTIs owing to their weak immune systems and prolonged disease length:

> *'I guess as a doctor, like I've already talked about, you may worry more than an elderly patient may recover less easily or be able to fight an infection as easily and therefore you're more likely to prescribe in an elderly patient.'* **(GP9: 30, female, 2 years)**

***5.3.1.1.1.2.3 Responsibility of other HCP***

In terms of the responsibility of other HCPs, this factor was highlighted by one of the participants (N = 1). The participant spoke about other HCP who work in walk-in centres and provide antibiotic prescriptions outside GP surgery hours. This participant expressed his frustration with this conflict in prescribing, especially when patients become demanding:

> *'These people then find another way of getting it so they don't get … It doesn't mean to say I'm going to give it. Many times I've not and I'm quite pleased that I haven't done that but they will go to say to a walk-in centre or they'll go to any. I get the discharge summary two days later, they managed to get antibiotics and that is a real source of frustration.'* **(GP7: 37, female, 6 years)**

#### *5.3.1.1.1.3 Others*

##### *5.3.1.1.1.3.1 Resistance*

Resistance was a seen by the majority of participants (N = 13) as one of the strongest factors that can influence and impact antibiotics prescribing. Participants used words such as *'resistance'* and *'sensitivity'* to address the influence of this factor. Being one of the widespread problems involving antibiotics, resistance was discussed by the participants from three different views: understanding resistance as a threat that mandates judicious prescribing, undertaking microbiological resistance tests, and seeking information about local resistance patterns.

The following quote emphasise the first view, which focused on GPs' understanding of and belief in resistance as a threat that should be considered during antibiotics prescribing:

> *'I think there is a physician perspective. It influences your decision; particularly how much you buy into current theories about antibiotic resistance, and some GPs are very worried about antibiotic resistance; some GPs think it doesn't apply to them and are very unworried about antibiotic resistance.'* **(GP2: 58, male, 29 years)**

This participant discussed the resistance from the second viewpoint, which related to microbiology resistance results:

> *'Essentially my current practice tends to be give the first-line antibiotic. If it's not responding, the second-line antibiotic. I tend to get an MSU, a urine sample for cultures and sensitivities and I give them the second-line. If it's not responding to the second-line then I have the answer by five days in terms of what the urine cultures say.'* **(GP16: 42, male, 4 years)**

The third view, which related to information about local resistance patterns, was reported by these two participants in answer to the question about factors influencing their prescribing practice:

> *'I think information is going to affect my prescribing. Antibiotic resistance and sensitivities…. information like it's going to be what has a high of degree of sensitivity; in other words, what antibiotics work locally. If something is becoming so useless to prescribe, then we don't want to be giving something that's not going to work in the vast majority of patients.'* **(GP11: 50, male, 22 years)**

*'What are the pattern of resistance of the antibiotic locally and nationally?'* **(GP17: 67, male, 14 years)**

### *5.3.1.1.1.3.2 Concerns*

Several participants (N = 10) demonstrated a high level of responsibility towards patients' drug safety, drug practicability and patient compliance by considering these concerns as major contributors to the factors influencing their antibiotic prescribing in adult and elderly. Participants used words such as *'side effects'*, *'tolerability'*, *'interactions'* and *'compliance'*. The following quotes from different participants' interviews were used to support the influence of side effects such as allergy on GPs antibiotics prescribing:

> *'If they say, 'oh, I had an allergy or vomited with that or I had a bad rash,' that might influence it. I'm trying to remember what medicines they're on, if they're on things like statins and just advising them. Sometimes I forget which ones to tell them to stop so I tell them, "Once you're started on the antibiotics, stop your statin for a week," because actually it's much easier to do that and they understand to that as well, these sorts of things.'* **(GP7: 37, female, 6 years)**

> *'What's the side effect profile likely to be? What's the tolerability of the medicine?'* **(GP4: 33, female, less than a year)**

> *'Side effects. Thinking about metronidazole. Drugs that can give you side effects'* **(GP10: 33, female, 2 years)**

The following quotes from different participants' interviews were used to support the influence of drug-drug interactions, practicability and compliance as a part of GPs concerns on antibiotics prescribing for elderly patients:

> *'I think with elderly patients; I suppose we just are more conscious of prescribing for elderly patients because of the possibility of it more medication interactions.'* **(GP4: 33, female, less than a year)**

> *'I always thinking about how the practicalities of taking the pills, whether it's BD, it will be easier than QDS, things like that. Which I might think more about in an elderly person. I wouldn't be worried about that too much in a younger person, because I think they can just deal with it. That's one of the main differences.'* **(GP10: 33, female, 2 years)**

> *'Certainly I'm more likely to prescribe something that's BD rather than QDS because it's just easier taking it.'* **(GP12: 35, female, 5.5 years)**

> *'They're generally more complicated. So they'd probably consult more often, I think. And that's from a patient safety point of view. You'd be less likely to do an antibiotic prescription on the phone for an elderly person versus a younger person.'* **(GP14: 34, male, 5 years)**

> *'Compliance with antibiotics… is she or he going to take the medication on time. You have to be very careful with the antibiotic, make sure that you have advised them how much of the antibiotic, how many times a day and how to take it, with*

*empty stomach or full stomach with food or something.'* **(GP17: 67, male, 14 years)**

### *5.3.1.1.1.3.3 Diagnosis and Clinical Decision-making*

A few female participants (N = 3) considered diagnosis and clinical decision-making to be influencing factors in the practice of antibiotics prescribing. Participants used the words *'diagnosis'* and *'decision'* to elaborate on this. In the quotes below, three participants addressed diagnosis and clinical decision-making as important factors in antibiotics prescribing decisions:

> *'What clinical decision am I making about the patient?'* **(GP4: 33, female, less than a year)**

> *'The diagnosis that he or she has reached about which infection it may be whether antibiotics are absolutely necessary.'* **(GP7: 37, female, 6 years)**

> *'You've made a diagnosis.'* **(GP9: 30, female, 2 years)**

### *5.3.1.1.1.3.4 GPs' Ethos and Ethical Values*

GPs' ethos and ethical values in relation to antibiotics emerged in the interview as one of the factors that might influence antibiotics prescribing in primary care. Only one participant (N = 1) addressed these factors when she was asked the question:

> *'Well I think, it's your own motive, your own ethical values, your own motivation for doing your job…. your own values and ethos about antibiotic prescribing and the time you have with your patient to explain that'* **(GP6: 40, female, 12 years)**

### *5.3.1.1.2 Theme 2: Extrinsic Factors (Patient-related Factors)*

Factors within this theme were discussed by the majority of participants as being key driving factors in their antibiotics prescribing. The following section discusses these factors in detail with the use of appropriate quotes from participants' interviews.

### *5.3.1.1.2.1 Patients' Age and Gender*

Age and gender were stated by a few participants (N = 2) to be elderly patient-related factors that might influence antibiotic prescribing as seen in the following quotes:

> *'Obviously there's the patient's individual factors…. their age and their gender'* **(GP15: 33, female, 3.5 years)**

> *'The factors, the age of the patient'* **(GP17: 67, male, 14 years)**

#### *5.3.1.1.2.2 Patients' Medical History and Clinical Characteristics*

Several participants (N = 8) considered this factor to be a key aspect of antibiotics prescribing. This aspect was often described by participants as being based on multiple factors including previous medical history, clinical presentation such as signs and symptoms, co-morbidities, frailty and severity of the infection. Utterances such as *'symptom'*, *'presentations'* and *'co-morbidity'* were used frequently by participants to express this factor.

This quote highlights the factor of patient presentation, which was mentioned many times during the interview owing to its importance:

> *'I suppose really again it's about how is the patient presenting.'* **(GP4: 33, female, less than a year)**

In the following two quotes, co-morbidities were the centre of the discussion by these two participants as a major factor in antibiotics prescribing using different utterances to refer to them:

> *'Well it's the clinical pictures the main thing and then secondly is what co-morbidities you're dealing with'* **(GP5: 45, male, 9 years)**
>
> *'Obviously there's the patient's… other medical problems'* **(GP15: 33, female, 3.5 years)**

This participant focused on patients' medical history by considering infection recurrence and the presence of underlying conditions that could predispose patients to more serious infection as part of this factor:

> *'I suppose… prior medical history, have they had recurrent infections that have been proven to be bacterial? Have they got underlying illness that might predispose them to developing a more serious infection and those sorts of things.'* **(GP6: 40, female, 12 years)**

Another participant used the word *'symptoms'* many times when discussing the factors influencing antibiotics prescribing:

> *'Based on what are the symptoms they've got'* **(GP15: 33, female, 3.5 years)**

Two participants considered elderly patients' characteristics and medical history as a key aspect of antibiotics prescribing.

This quote by one male participant emphasises GPs' level of awareness of elderly patients' co-morbidities and its influence on antibiotics prescribing to avoid further aggravating patients' condition. The participant used diabetes and dementia as examples to highlight this factor:

> *'Some doctors are more aware of the implications of co-morbidity than others, and particularly poorly-controlled diabetes and it often doesn't take much to tip an elderly patient with co-morbidity over the edge into much more serious illness, particularly if you've got a mild dementia. It just takes a simple infection, and the mild dementia will become acute confusion … most elderly patients, as I said before, are going to need an antibiotic… and the more you can treat problems early, the less you end up with them having to see specialists for treatment of their multi-morbidity.'* **(GP2: 58, male, 29 years)**

Another quote by a female participant focused on elderly patients' co-morbidities and frailty as factors that can encourage her antibiotic prescribing:

> *'The fact that they might have renal impairment, be on other medications and other medical problems I might ... that's a difficult one because like I said before if it's a younger woman it's often a lot more obvious from their symptoms that they've got a UTI, but in an elderly patient because they're more frail I might be more tempted to prescribe. It's difficult, it's really case by, case by case I would say.'* **(GP15: 33, female, 3.5 years)**

#### *5.3.1.1.2.3 Patients' Social Situations and Living Conditions*

Patients' social situations and living conditions were seen by a few participants (N = 2) as influential factors in that they might encourage or discourage a prescription as well as the choice of antibiotic. Words such as *'social'* and *'living'* were used by participants to elaborate on these factors.

One participant mentioned social situation and social factors in her answer to the question:

> *'Their social situation as well. They need some support. Yeah, I think the physical, mental and social factors of the patient need to be taken into consideration when you're prescribing.'* **(GP3: 35, female, 5.5 years)**

This participant explained his genuine concerns about knowing his patients' social situation and living conditions as he linked them to the process of antibiotic administration:

> *'Social situation of the patient, living alone… For the social side of it, if patient is living alone, has there somebody to care her, is she aware that she should take antibiotic this time of this or that. The patient's point of view, as I said that if they are capable of taking the antibiotic and are aware of the duration or doses of the antibiotics, so each factor has to be ... just carefully.'* **(GP17: 67, male, 14 years)**

One of the participants who addressed social situation and living conditions in his previous answer repeated the same factor when he highlighted the factors related to elderly patients with UTIs, since these patients might need support by other individuals:

> *'The elderly patient sometimes depends on the carer, it depends if they're living alone, they forget, they have got co-morbidity, there's a huge difference from them or somebody has got UTI and works in office and every six hours remembers to take medication, no problem… again, it's because of the social situation…again social situation with the patient that I've mentioned several times that may affect the choice of antibiotics.'* **(GP17: 67, male, 14 years)**

### *5.3.1.1.2.4 Patients' Level of Understanding and Knowledge*

Only a few participants (N = 3) addressed patients' level of understanding and knowledge as a factor that influences their antibiotics prescribing. Words such as *'understand'* and *'informed'* were used by participants to discuss it.

The following two quotes by participants who used the word *'people'* to refer to patients explain how lack of knowledge and understanding about antibiotics activity is a driving factor in antibiotics prescribing:

> *'I think a lot of people don't know really that antibiotics only work on bacteria … People's knowledge as well and understanding.'* **(GP10: 33, female, 2 years)**

> *'Also, what they understand about virus versus bacteria. That would kind of influence it as well.'* **(GP14: 34, male, 5 years)**

The following quote explains how informed and educated patients can be less likely to demand an antibiotic when it is deemed to be unnecessary:

> *'I think the uneducated will come in and just go, 'I need medicine. I need medicine.' There's an element of often the uneducated will just come and want medicine, and medicines, they'll mean antibiotics… I think if you're informed and educated, no matter where you're from, you'll probably go, 'Do I really need treatment? Is there anything I can do that will get me better without taking a drug?' I think often the well-informed and the educated will try and avoid taking unnecessary drugs, whereas the uneducated love to take drugs.'* **(GP11: 50, male, 22 years)**

A few participants (N = 3) addressed the level of patients' understanding and knowledge as a factor that influences their antibiotics prescribing in elderly patients with UTIs. This quote by one female participant explains how elderly patients being able to understand the signs and symptoms of UTIs can be very useful with regard to early management:

> *'I think the only thing is just again if somebody had a UTI before and they've had lot of UTIs, they'll know that they'll come early probably to talk to us about it… I*

*think it can be a very useful thing. It can also be a challenge as well.'* **(GP4: 33, female, less than a year)**

Another participant explained how a lack of knowledge about UTIs in elderly patients can influence their awareness of the necessity of antibiotics:

> *'Well, I think that's a bit more difficult because then they might have less concept of when they should be on antibiotics or not. Obviously, if somebody doesn't have the internet, they can't look up guidance, so they can't look up information on that.'* **(GP14: 34, male, 5 years)**

#### *5.3.1.1.2.5 Patients' Desire for a Quick Fix*

One participant (N = 1) focused on patients' desire for a quick fix as a factor affecting antibiotics prescribing. GPs might find themselves under pressure from the patient to prescribe antibiotics for a quick fix to meet a prescheduled activity, occasion or event such as travelling or a holiday. This can happen quite often, according to the participant:

> *'Are they going on holiday in two days and they want to get better quickly? That's often the reason for the patients wanting them as well.'* **(GP6: 40, female, 12 years)**

#### *5.3.1.1.2.6 Patient's Autonomy*

This factor was highlighted by a few participants (N = 3) only when they discussed the case of elderly patients with UTIs compared with the general population. Terms such as *'less willing'* and *'you are the doctor'* were used by participants to describe this factor.

In this quote, the participant explained how elderly patients are usually less willing to be involved in the processes of prescribing and decision-making, preferring GPs to make the decision on their behalf:

> *'I think elderly patient generally speaking are, this is very general It is a generalisation but of course there are exceptions to this rule. I think elderly patients are generally more and willing to accept your decision as their decision. Perhaps you find them sometimes less willing to be part of the decision-making process themselves. They want you to make the decision for them. There's only a certain some type of elderly patients.'* **(GP4: 33, female, less than a year)**

A second participant elaborated on this attitude of elderly patients, suggesting that it might be because elderly patients grew up in a culture and time when patients' autonomy was not discussed extensively:

> *'The patients who tend to have very clear expectations and agendas don't tend to be the elderly patients not to say, I think elderly patients tend to be … I don't know whether it's just because that's how, I mean, I think, elderly people have a culture*

*with doctors where they're perhaps more likely to challenge doctors but they certainly tend to be more directed by what the doctor says rather than what they've come in with, with the expectations they come in with. I think elderly patients are much more likely to be happy with whatever prescribing decision is made by the doctor. I think there's been a cultural shift, I mean I think some of the elderly patients are 70, 80, 90, will have grown up in a culture where patient autonomy wasn't even really discussed. When the doctor would make decisions on the patient's behalf without really very much consultation with the patient and that was the norm probably until about 30 or 40 years ago. They've grown up in that culture. It may also be that older people are generally less bolshie than younger people. Also, those younger are used to getting a lot more information and has a lot more access to information which maybe some o people don't make so much use of. Younger people will have often looked online and they come to their own decisions but they will certainly be expecting the doctor to sit up and listen to what they've got to say. Whereas older people will sometimes find it a bit strange if you ask them what they think, they will sometimes say, 'Well, you're the doctor.' I think it's about cultural shift really.'* **(GP13: 45, male, 18 years)**

#### 5.3.1.2 Category 2: Meso-Level Factors

In this category, themes related to the practice/surgery or CCG context were the key components discussed. The category comprises four factors, namely, visits and education by advisors; auditing, monitoring and feedback on prescribing; influence of secondary care doctors' practice; and implementation of local policies, guidance and formulary.

##### *5.3.1.2.1 Theme 1: Visits and Education by Prescribing Advisors*

A few participants (N = 2) discussed the influence of prescribing advisor visits to discuss and educate GPs who tend to prescribe loads of antibiotics frequently. The participants used the word *'advisor'* to describe this factor. This participant explained how over-prescribing antibiotics can result in a visit by a prescribing advisor to discuss with the prescribing GP the reason behind the behaviour, which can end up flagging the GP owing to inappropriate prescribing:

> *'We all know it's not good to over-prescribe, so I think if you are prescribing loads of antibiotics, your prescribing advisor might come and talk to you about that or saying why you're prescribing all these medications and it would be flagged up and you'd have to look at that.'* **(GP6: 40, female, 12 years)**

The second participant acknowledged the educational role of the prescribing advisor in influencing GPs' prescribing behaviour:

> *'To educate us when we are using antibiotic and keeping reminding us what antibiotics available, what is the benefits of the antibiotics, why should change*

> *from this medication to that medication, why, what are the pattern of resistance of the antibiotic locally and nationally?.'* **(GP17: 67, male, 14 years)**

#### *5.3.1.2.2 Theme 2: Audit, Monitoring and Feedback on Prescribing*

Several participants (N = 5) stated that audit and feedback are strong factors that might influence their antibiotics prescribing. Participants used different utterances to highlight this factor such as *'audit'*, *'monitoring'* and *'feedback'*.

This participant explained the use of the electronic prescribing system and its role in the auditing of antibiotics prescribing, which can raise questions about any detected high prescribing rate and pattern:

> *'I think certainly with, in primary care with the use of ePACT, look at your own prescribing and patterns and seeing how you compare with another, those can be useful. I think that it's much more useful to, so I think those, I think when you audit, that definitely does make you think, oh, yes, I might do more than my partners.'* **(GP1: 46, female, 24 years)**

This participant explained the influence of CCG on prescribing through medicine management teams, which mainly work to control budgets:

> *'There's that influence from the CCG, back to the medicine management advisors. They have a strong influence on our prescribing, but it's largely a budgetary influence.'* **(GP2: 58, male, 29 years)**

Another participant acknowledged auditing and feedback as being helpful in identifying her personal prescribing practice for confirmed UTIs:

> *'Peer review… and feedback from outside sources… having personal feedback about actually how many of those I treated had a confirmed UTI, because you can't really do that with a respiratory tract infection, but you could do it with urinary tract infections. That would be helpful feedback for me.'* **(GP3: 35, female, 5.5 years)**

One participant considered audit and feedback very helpful especially in comparing prescribing between local practices, which could raise questions about specific prescribing behaviours and even suggest reasons for them:

> *'We're often given charts of our prescribing compared to local practices which are helpful, see if where prescribing more or less than for the same population. It's good to look at those things, we look at them question why you're doing that and what are the reasons looking into that, doing audit.'* **(GP6: 40, female, 12 years)**

Another participant explained the influence of pharmacy advisors and their duties, which include giving feedback on antibiotics prescribing patterns:

> *'Feedback from pharmacy advisers and looking through prescribing patterns.'* **(GP13: 45, male, 18 years)**

#### *5.3.1.2.3 Theme 3: Influence of Secondary Care Doctors' Prescribing Practice*

Secondary care prescribing appeared as one of the factors that can have an influence over GPs' prescribing of antibiotics. A participant who acknowledged this factor used *'secondary care doctor'* to refer to it. The following participant expressed her annoyance with secondary care doctors' prescribing attitudes, which have an influence on GPs' antibiotics prescribing:

> *'Obviously secondary care requesting something to be prescribed which might not be things you exactly prescribe. Then there's somethings, some tension there and some challenges between what secondary care doctor wants to prescribe and what primary care can prescribe and evidence-based surround it… This might be inappropriate to say, but as it's confidential I feel there's more maverick behaviour… I feel the problem with secondary care doctors are more willing to step outside the guidelines or feel that they can because that's their area of special interest. They might have learned about the newest drug or whatever more than primary care doctors do normally, because of what they're guided on. Also with regard to their knowledge, you might not be up to scratch with the latest, the newest antibiotic for 'x' condition compared to the specialist doctor in hospital… Yeah, I think it happens quite often, yeah. Yeah, often enough to cause a bit of a headache to have that conversation with the patient or try to contact the doctor in the hospital and see who he is, because sometimes it's a younger doctor who doesn't know or sometimes it's a locum doctor who's come from elsewhere. Yeah, it's reasonable, yeah. Yeah, it does happen. I'm sure there's GPs that do it as well, but from the GP side of things I feel it often comes from off secondary care… Also it can set a bad example because frankly, regular doctors are regularly doing and primary care doctors might start to think that it's okay for them to do it, because they've read the latest advice. The newest journal, the newest drug or some advert for medication.'* **(GP3: 35, female, 5.5 years)**

#### *5.3.1.2.4 Theme 4: Implementation of Local Policies, Guidance and Formulary*

Several participants (N = 9) addressed implementation of local policies, guidance and formulary as a factor that can influence their prescribing. Participants used the words *'policy', 'local guidance' and 'formulary'* to explore this factor.

The following quotes describe the influence of local guidance, policy and formulary on participants' antibiotics prescribing:

> *'I'd say I think the factors that influence it are probably changes in guidelines, or formulary within an area that you're practicing in… I think that again goes back*

*to those kind of wide policy that says you need to prescribe this, or availability of particular drugs changes, and you can't prescribe certain drugs. I think those would all influence it, if there was any, yeah, I think those would be the key ones, I would say.'* **(GP1: 46, female, 24 years)**

*'Local antibiotic prescribing guidance, which should be available via your CCG or iPhone, Apple, whatever they have for that, which might be the same as the national guidance or it might be slightly different in some ways. So you always have to look at both, really.'* **(GP14: 34, male, 5 years)**

*'The choice of antibiotic is down to for me anyway local antibiotic prescribing guidelines which are based on local sensitivities... When it comes to guidelines and stuff and when it comes to antibiotics I do tend to stick to them in particularly if they're local guidelines for antibiotics because they're supposed to be based on local sensitivities.'* **(GP15: 33, female, 3.5 years)**

#### 5.3.1.3 Category 3: Macro-Level Factors

In this category, themes related to society or to the national healthcare system were the key components discussed. The category consists of 10 factors, namely, time, guidelines and evidence, drug availability, incentives, media, cost, healthcare resources and constraints, pharmaceutical companies, over-prescribing, society influence and expectations, and lack of differences between adults and the elderly.

##### *5.3.1.3.1 Theme 1: Time*

Lack of time during consultations was stated by a few participants (N = 2) as one of the factors that can influence antibiotics prescribing. The participants used the word *'time'* to discuss their viewpoint. The average reported consultation time ranged between 10 and 20 minutes.

The following quotes by two participants discuss how time as an aspect can be an important factor in making an informed decision about antibiotics:

*'I guess to having enough time to make the informed decisions so technical history and examination, having urine analysis, to be able to do the dipstick, having he patient's history in front of you so you can know they frequently have UTIs or if you don't they can help inform you. You need to have the time for that'* **(GP3: 35, female, 5.5 years)**

*'Time you have with your patient to explain that.'* **(GP6: 40, female, 12 years)**

#### *5.3.1.3.2 Theme 2: Guidelines and Evidence*

Many participants (N = 11) said that guidelines and evidence can have a strong impact on their antibiotics prescribing. Participants used the words *'guidelines'* and *'evidence'* to discuss these factors.

A quote by a female participant highlighted the impact of frequently updated antibiotics guidelines on prescribing decisions:

> *'I think especially for antibacterial prescribing there's a lot of guidance available and that's which is constantly updated I think and all have a big impact.'* **(GP4: 33, female, less than a year)**

These two participants mentioned that guidelines are a factor that can influence their antibiotics prescribing:

> *'I think it's going to be guidelines coming from above. It's going to be things like Department of Health guidelines, NICE guidelines.'* **(GP11: 50, male, 22 years)**

> *'Then what you've read in terms of evidence-based guidelines or literature.'* **(GP13: 45, male, 18 years)**

This participant explained how his antibiotics prescribing is influenced by the evidence and national guidelines published by the national healthcare organisations:

> *'It comes back to your… the overall kind of national guidelines. I'm talking about obviously you've got national guidance, which tells you what the evidence basis for ... based on research evidence papers on what antibiotics to use in UTI, but then also that's national evidence… It's much more about what's the research evidence, national guideline evidence for decision-making, and also key stakeholders or local GPs, NICE, Public Health England, that sort of people.'* **(GP14: 34, male, 5 years)**

#### *5.3.1.3.3 Theme 3: Antibiotics Shortage*

Drug shortage was addressed as one of the factors influencing antibiotics prescribing by several participants (N = 7). Words such as *'availability'* and *'shortage'* were used to highlight this factor. The following quotes by participants highlight the availability of antibiotics as one of the factors that influences their antibiotics prescribing:

> *'What's available? What antibiotics … You know something might be in short supply and suddenly we can't use it. Yeah.'* **(GP7: 37, female, 6 years)**

> *'Availability. Sometimes, not so much of antibiotics, but every now and then you get things that are not available … There's a supply problem.'* **(GP12: 35, female, 5.5 years)**

*'If there's a natural shortage of the antibiotic, that will also change what I'm doing as well which happens. Yes, the pharmacists run out of antibiotics running out of the antibiotic. Then I'll give whatever else they have in stock… It depends. It's just periodic in terms of certain types of medications, it can happen. I think there was recently a shortage of chloramphenicol. I think there was a point where something odd happened like that … and there was just a lack in supply. It happened for a couple of weeks and then it sorts itself out. It's got to do with the manufacturing of the pharmaceutical companies rather than my side. I get to know about it when the patient comes back from the carrier saying they don't have this available.'* **(GP16: 42, male, 4 years)**

#### *5.3.1.3.4 Theme 4: Incentives*

Only a few participants (N = 2) focused on incentives as one of the factors that affects antibiotics prescribing. Participants used the word *'incentive'* to describe their interest in this factor. In this quote a participant discusses how a prescribing incentive can have a role in reducing and influencing antibiotics prescribing in general practice:

*'I guess there's sometimes financial incentives that are more targeted at practice partners, but obviously trickled down to the salary doctors about reducing prescribing… incentives to reduce prescribing I think all affect prescribing'* **(GP3: 35, female, 5.5 years)**

A second participant talked a lot about the incentive scheme during the interview and explained his own point of view by discussing the positive impact of taking part in this system:

*'Well, as a GP, you've got to consider your budget and also incentive scheme… I think it helps particularly with antibiotic prescribing because whenever you prescribe antibiotics, you have to think is it one of the top ten that we are asked to prescribed from… Maybe these prescribing incentive schemes I think play an important role... There's incentives or disincentives for poor prescribing or incentives for good prescribing and that's a driver.?'* **(GP13: 45, male, 18 years)**

#### *5.3.1.3.5 Theme 5: Media*

Media was urged by a few participants (N = 5) as being one of the factors that could affect antibiotics prescribing through influencing patients and the public. Participants used the words *'TV', 'radio', 'Internet'* and *'newspapers'* as the main channels for this factor.

One participant commented on the role played by the media and how it shaped society's perspective with regard to antibiotics demand and resistance patterns:

*'Working up from sort of a patient level so patients experience their own personal... the things that they read in the newspapers, see on television and those*

> *thing I think that society's perspectives are very much shaped these days by the media as I said before… I think that in terms of antibacterial prescribing, I think people are more conscious now of patterns of resistance. Some sets of patients who are very responsible about that and are aware of it and will come and say, 'I don't want to add to that problem.'... I think the media has a lot of role to play in terms of that.'* **(GP4: 33, female, less than a year)**

Another participant described the effect of TV and radio on patients' own views:

> *'Also, things that happen… in TV that can also make a big difference as well when the patients come in. Or things they've heard on the radio. All these sort of things can have big impact.'* **(GP16: 42, male, 4 years)**

#### *5.3.1.3.6 Theme 6: Cost*

Many participants (N = 8) stated cost to be one of the strongest factors affecting their prescribing practice. Participants tended to use words such as *'cost'* and *'cost-effectiveness'* to describe this factor. Antibiotics costs were viewed from two different perspectives, namely, acquisition (purchase) cost and cost-effectiveness.

The following quotes by several participants look at antibiotics cost from an acquisition cost point of view. Within this perspective, two different views were identified based on participants' interpretation. On one hand, a group of participants respected the economic value of antibiotics in general; on the other hand, a second group of participants underestimated the cost of antibiotics and therefore considered it a minor factor:

> *'The cost of the drug'* **(GP3: 35, female, 5.5 years)**

> *'What's the cost as well… Is it a hugely expensive drug you know to prescribe in the first place?'* **(GP4: 33, female, less than a year)**

> *'Also, cost comes into it as well… Well I guess… there is always some cost considerations that have been taking into consideration'* **(GP15: 33, female, 3.5 years)**

These two participants addressed the perspective of the cost-effectiveness of antibiotics with contradictory opinions:

> *'I guess my decision is based on… what is cost-effective'* **(GP8: 36, male, 2 years)**

> *'For these drugs, I don't think cost-effectiveness really comes into it, unless, obviously, we've got a new drug and it's really expensive.'* **(GP14: 34, male, 5 years)**

#### *5.3.1.3.7 Theme 7: Healthcare Resources and Constraints*

Two participants (N= 2) described healthcare resources as influencing factors on antibiotics prescribing. Words such as *'health economy'* and *'constraints'* were mentioned when describing this factor. The following quotes by two participants discuss the downside of healthcare resource constraints on patient treatment under the factors influencing their antibiotics prescribing practice:

> *'It's that awareness of the overall health economy ... that all of us in general practice are trying to reduce A and E attendances, so you want to treat the problem in primary care and not have the embarrassment of the person failing to have adequate treatment in primary care and turning up in Casualty.'* **(GP2: 58, male, 29 years)**

> *'Who's funding things? What budge re-constraints there are?'* **(GP7: 37, female, 6 years)**

#### *5.3.1.3.8 Theme 8: Pharmaceutical Companies*

Pharmaceutical companies can play an important role in influencing the prescribing process in general. Only one participant acknowledged the influence of this factor during interviews. However, in the case of antibiotics the influence is minimal, as highlighted by this participant who mentioned the role of pharmaceutical companies as one of the influencing factors:

> *'We prescribe as influenced sometimes by drug companies but in antibiotics, not very much.'* **(GP13: 45, male, 18 years)**

#### *5.3.1.3.9 Theme 9: Over-prescribing*

Only a couple of participants (N = 2) elaborated on over-prescribing as one of the factors that influences their antibiotics prescribing. The word *'over-prescribing'* was stated by both of them. The following two quotes illustrate the effect of over-prescribing on GPs' antibiotics prescribing:

> *'Well the main thing that influences me is the concern about over-prescribing.'* **(GP5: 45, male, 9 years)**

> *'We all know it's not good to over-prescribe, so I think if you are prescribing loads of antibiotics, your prescribing advisor might come and talk to you about that or saying why you're prescribing all these medications and it would be flagged up and you'd have to look at that.'* **(GP6: 40, female, 12 years)**

##### *5.3.1.3.10 Theme 10: Society's Experience and Expectations*

The influence of society and public experience of antibiotics prescribing were mentioned by a few participants (N = 5) who used utterances such as *'society'* and *'people'*. The following three examples of participants support the influence of this factor on GPs' antibiotics prescribing practice:

> *'I think within what people's previous experience, people's experience of prescribing in their immediate family or friends that will normally determine … Because there'll be a conversation, someone is ill and they think, 'Do I need antibiotics?' Normally we come to the discussion which happens at home or with someone they trust or a partner or parent or whoever, there'll be some conversation about should I go and get antibiotics? That's very much based on people's own experience. If people are very used to the fact that if you've got a sore throat and you go and get the antibiotic, they will only advice either a friend or relative to do the same.'* **(GP13: 45, male, 18 years)**

> *'I think society wants to get better and I can understand that and so if there's a treatment that is out there that potentially will work, they will want to ask for that. Again, if they're aware of things, if they feel that they're able to ask for such in treatments, then that will affect their … That potentially could affect the prescription.'* **(GP7: 37, female, 6 years)**

> *'General societal beliefs about antibiotics'* **(GP14: 34, male, 5 years)**

However, only two participants considered this factor when they discussed elderly patients with UTIs. The following two quotes explain the influence of society's expectations and attitudes on antibiotics prescribing in the case of elderly patients with UTIs:

> *'I think there is common knowledge in society that antibiotics will help a urine infection in somebody who's elderly. It's not just the Internet generation. Elderly people generally are aware of that.'* **(GP2: 58, male, 29 years)**

> *'I suppose it sometimes is relative that you worry or society worries more about a younger child or a young woman versus an elderly patient. I think that those ageist attitudes exist, so they might influence behaviour.'* **(GP3: 35, female, 5.5 years)**

Two participants (N = 2) considered that all the factors that influence antibiotics prescribing for elderly patients are the same as those that relate to adult patients and, if present, they do not differ much, as suggested by these two participants:

> *'I don't think there's much in terms of differences. You go through still the same process of what the diagnosis is, has there been a change in the policy locally, what was their previous history been, have they had antibiotics recently. So that*

*might influence it, if they've already had one set of antibiotics, then you might be much more mindful of waiting'* **(GP1: 46, female, 24 years)**

*'I don't think so because other than being mindful that elderly patients have a different sort of physiology perhaps, a different blood test but you use what is in front of you. It could be the same. I might have a 30-year-old who's got a renal transplant and it has low renal function or that they have ... I still need to look at the blood test, the co-morbidities, so no... I think it's the same criteria… On the whole I think society still wants the same things. They want the treatment that will make them better and it doesn't necessarily matter if they're older or younger'* **(GP7: 37, female, 6 years)**

## 5.4 Discussion about Thematic Analysis of Factors Influencing GPs' Prescribing of Antibiotics for UTIs

The application of phenomenographic, semi-structured interviews with thematic analysis identified numerous factors that might influence GPs' antibiotics prescribing for UTIs, which is complex and involves GPs, patients, local practices and CCGs as well as the healthcare system. This section discusses these factors in relation to the literature reviewed earlier in Chapter Two.

### 5.4.1 Micro-Level Factors

In this analysis, the micro context was found to include several factors related to individual GP–patient interactions. Within this context, GPs addressed a number of factors that were sub-categorised into intrinsic factors, related to GPs, and extrinsic factors, related to patients.

#### 5.4.1.1 Intrinsic Factors

One of the intrinsic factors found to influence GPs' antibiotics prescribing was their personal experience and familiarity with specific antibiotics. This was stated by several GPs (N= 6) to be one of the strongest factors that might impact antibiotics prescribing. GPs' personal experiences might direct their actions spontaneously towards or against prescribing, as addressed by some of them. GPs who tended to prescribe under the influence of this factor often prescribed from a range of antibiotics they knew well. Familiarity with certain antibiotics can make GPs feel comfortable and confident about the antibiotic they are prescribing. Personal experience and familiarity as factors could result from the knowledge the GPs developed during their undergraduate study and the previous experiences they gained during their postgraduate training and years of practice. These findings were in line with other qualitative literature reviewed (Kuehlein *et al.* 2011, Vazquez-Lago *et al.* 2012). Being a common factor, this might explain why GPs tend sometimes to prescribe specific antibiotic(s) or altered durations against recommendations. This finding can explain why there are variations in antibiotics prescribing practice among GPs, which was consistent with the findings from the DUR study in this research with regard to GPs' non-adherence as well as the variations in GPs' perceptions and views as found in the phenomenographic analysis.

GPs' undergraduate education, knowledge and postgraduate training were said to be a key influencing factor in antibiotics prescribing (N = 6). However, antibiotic pharmacology was not given enough weight in the undergraduate curriculum, as one of the academic GPs in this study commented. Furthermore, another GP stated that an elderly rotation was only elective training for GPs. It was found that little curricular time was devoted to elderly patients' pharmacology and that educational programmes have not been thoroughly evaluated. This was reported by one systematic review aimed at exploring the quantity and nature of geriatric pharmacology education in undergraduate (12 hours) and postgraduate curricula for GPs (11 hours) including the UK (Keijsers *et al.* 2012). The study finding with regard to the influence of education on prescribing was similar to that reported by Kuehlein *et al.* (2011), who described this factor as a key driver for GPs' prescribing behaviour and by Teixeira Rodrigues *et al.* (2013), who reviewed the influence of this factor in five studies and identified a direct link. Moreover, this factor was also described as one of the external horizon findings in the phenomenographic analysis, which could explain why changing GPs' prescribing behaviour can be challenging. Although these findings might suggest the need for incorporating more educational interventions aimed at increasing the level of knowledge about elderly patients and antibiotics in terms of prescribing, no course would entirely change GPs' prescribing practice.

Another strong factor that might influence GPs' attitudes to prescribing antibiotics was complacency, which was discussed by all of the interviewed GPs (N = 17), suggesting the dominant influence of this factor on GPs' antibiotics prescribing practice. This factor was found to originate from patients, family members, carers and even GPs themselves as reported by GPs in this study and found by two systematic reviews (Lopez-Vazquez *et al.* 2012, Teixeira Rodrigues *et al.* 2013). Complacency was described by GPs as being a very uncomfortable attitude that can make some of them feel they have to prescribe antibiotics to avoid any kind of confrontation or tension, to maintain the GP–patient relationship, or to end consultations with demanding patients. Greater patient expectation can be driven by prior experience of receiving an antibiotic during a consultation or falsely assumption by GPs that patient expect an antibiotic and to satisfy patients who expect antibiotics as expressed by GPs in this study. Therefore, improving GP–patient communication can play a major role in reducing the influence of complacency, as communication may reduce inappropriate or unnecessary antibiotics prescribing. This is evident from the findings of qualitative, semi-structured interviews with 20 GPs from the UK aimed at exploring GPs' views and experiences about communicating with their patients, with a focus on the problem of expectations of antibiotics as a possible treatment (Mustafa *et al.* 2014). The finding about complacency in this study was found to be in agreement with the reviewed literature (Bjornsdottir and Hansen 2002, Petursson 2005, Kotwani *et al.* 2010, Vazquez-Lago *et al.* 2012, Bjorkman *et al.* 2013, Teixeira Rodrigues *et al.* 2013) and also with the phenomenographic analysis of GPs' views in this research. Although these studies support the influence of complacency on GPs' prescribing, conflicting opinions have been reported in other qualitative research that comments on this factor having little or no influence on GPs prescribing (Paredes *et al.* 1996, Bjornsdottir *et al.* 2010). However, these findings were based on old data, including Bjornsdottir *et al.* (2010), who used data from 1995. The recent shift in practice towards more patient-shared decision-making might have augmented the influence of complacency on GPs' prescribing. Additionally, differences in countries' regulations for purchasing antibiotics without prescription could explain this conflicting opinion. Interestingly, GPs discussed this as a disturbing factor in adult patients. However, they considered it to be a very useful, acceptable and appropriate approach when dealing with elderly patients and their carers or family members since elderly patients often have trouble vocalising their problems, hardly visit their GPs and are more susceptible to UTI complications. This finding was found to be novel since no previous work has studied the influence of complacency on GPs' antibiotics prescribing for elderly patients. Further research is indicated to explore the influence of antibiotic complacency for elderly patients, elderly carers and family members.

Fear was another factor within the micro context, related to a restrictive prescribing attitude and possible future complications arising from withholding antibiotics (N = 2). Fear was discussed as a factor in adult patients by one GP, although when it came to giving an illustration she chose a same-day case involving a mother and child. Another GP discussed this factor from the perspective of elderly patients. Fear can be seen in this study in two different scenarios: where the GP has fearful patients, carers or family members who transfer this feeling to the GP, and where the GP feels that prescribing antibiotics, although not indicated, might be in the best interests of patients, carers or family members. Both scenarios were highlighted and described by Petursson (2005) as a non-pharmacological reason for antibiotics prescribing by GPs. In both scenarios GPs are more likely to prescribe antibiotics. In this study fear as a factor was described in adult patients consistently with the first scenario, while the second scenario was described by GPs focusing on fear in elderly patients. The findings with regard to both scenarios were in line with those of Petursson (2005) in adult patients as a result of having a fearful patient or family member, conflict and discomfort, and fear about self-reputation and losing patients, of Vazquez-Lago *et al.* (2012) in elderly patients as a result of patient condition and characteristics and of Teixeira Rodrigues *et al.* (2013) in as a result of fear of developing more serious complications and fear of losing patients, which has been shown to be directly related to antibiotics prescribing. All these studies linked fears directly to antibiotics misuse. In this research, findings from GPs' perceptions in the phenomenographic analysis identified some GPs who described their antibiotics prescribing practice to be associated with low-threshold in elderly patients, which could be a consequence for their fears about elderly patients' conditions deteriorating. This could make fear one of the important factors that should be targeted in GPs' perceptions change.

In practice, the responsibility for antibiotics prescribing is assigned to GPs, but interestingly the role of other HCPs in this process was highlighted by one GP (N = 1) (non-medical prescribing). Prescribing by other HCPs such as nurses who work in walk-in centres (WIC) or out-of-hours (OOH) services was considered to be influential as some patients misuse the introduction of these services to obtain drugs such as antibiotics, as was reported in one qualitative study by (Carey *et al.* 2014), who conducted semi-structured interviews with 40 nurses who stated that some patients use immediate access services for medicines that should have been obtained through a GP. At present, it is not possible nationally to estimate antibiotics prescribing rates/volume via OOH. However, given the volume of activity, it is likely to contribute substantially to overall prescribing rates, as highlighted by a governmental report that estimated antibiotic courses prescribed by OOH general practice to be 2.2% of all medical antibiotics (and 1.9% by cost) based on antibiotics utilisation data from 2012–2013 (Pinder *et al.* 2015). This factor was perceived to create a status of conflict in prescribing as stated by the GP, as it can result in feeding patients' demanding attitudes, further increasing demand for antibiotics prescribing. Furthermore, antibiotics prescribing practices vary among these professionals in terms of threshold, volume and antibiotic choice, which can in some circumstances be second-line antibiotics when patients' conditions have deteriorated (Pinder *et al.* 2015). This prescribing practice and variations in prescribing by other professionals could be owing to worsening of patients' condition, avoidance of re-consultation or simply because of the workload. Additionally, WIC professionals tend to prescribe antibiotics without knowing patients' characteristics or medical history, which might affect patients negatively. This finding was found to be similar to those in the reviewed literature (Kotwani *et al.* 2010, Vazquez-Lago *et al.* 2012, Teixeira Rodrigues *et al.* 2013), which identified the presence of a direct relationship between the responsibility of other HCPs and antibiotics prescribing. However, GPs who stated this factor might want to share the responsibility or the blame of inappropriate antibiotics prescribing with other HCPs. To understand the impact of these services on antibiotics prescribing, further research aiming to estimate, audit and explore HCPs' antibiotics prescribing in WIC and during OOH services is indicated.

Resistance was seen by the majority of interviewed GPs (N = 13) to be a key factor affecting GPs' antibiotics prescribing practice. Being one of the most widespread problems with antibiotics, resistance was discussed in relation to understanding its meaning as a threat that requires judicious prescribing, results from microbiology laboratories and information about local resistance patterns. Overall, GPs who recognised resistance as a factor understood the risks and responsibilities associated with the impact of resistance on antibiotics efficacy, antibiotics treatment outcomes and society. Moreover, GPs who discussed resistance as a threat showed concern about those GPs who tended to believe that their antibiotics prescribing practice was unlikely to contribute to the development of resistance. GPs who considered resistance from a microbial perspective as well as local or national resistance patterns felt very comfortable when their prescribing was guided by laboratory cultures and sensitivity results, and when they could use knowledge of resistance patterns to minimise the risks and impact of resistance. The findings about resistance were consistent with those in much of the reviewed qualitative research (Bjornsdottir and Hansen 2002, Vazquez-Lago *et al.* 2012, Bjorkman *et al.* 2013, Duane *et al.* 2016), which found that the vast majority of GPs considered resistance an important factor in guiding prescribing in various degrees, in addition to showing a good level of understanding, awareness and knowledge about the negative consequences of resistance for those who prescribed rationally. Although the literature reported the presence of variations in understanding resistance, interventions aiming to narrow these variations should be promoted among GPs including personal audit and feedback for those with inappropriate prescribing.

In practice, GPs prescribe antibiotics to treat infections and reduce patients' recovery time from UTI symptoms by one to two days, as concluded in different studies (Little *et al.* 2009, Booth *et al.* 2013) and a systematic review (Milo *et al.* 2005). However, this must be balanced against the negative consequences of antibiotics. As with any drug, antibiotics are associated with risks relating to side effects, drug–drug interactions and patient compliance. In this study, several GPs (N = 10) demonstrated a high level of responsibility towards patients' drug safety, the practicability of any antibiotics regimen and patient compliance. GPs expressed uncomfortable or anxious feelings when they had limited choices of antibiotics with minimal risk, especially if patients expected or demanded different antibiotics. Interestingly, concerns as a factor was highlighted more in adult patients compared with elderly patients. Elderly people tend to have issues with memory, vocalising problems and using polypharmacy, thus extra caution should be applied when prescribing antibiotics for elderly patients (Corsonello *et al.* 2015). Additionally, education should take place more than once with consideration of proper methods of increasing patient compliance. This might be linked with GPs' backgrounds in elderly pharmacology and pharmacotherapy, in particular in relation to antibiotics. Findings about concerns were mainly discussed in the literature from a general safety and side-effects perspective. In this study the findings regarding safety and side effects were in line with Bjornsdottir and Hansen (2002), Petursson (2005) and Bjorkman *et al.* (2013) as a theme but not as a perspective, as GPs in this study discussed these issues from the point of quality of prescribing and awareness of antibiotics prescribing issues. However, in Bjornsdottir and Hansen (2002), Petursson (2005) and Bjorkman *et al.* (2013), GPs discussed side effects and patient safety in terms of fear of ADR consequences, as one of the main principles of medicine practice is *'do not harm'* (Kohn *et al.* 2000). This factor was also part of GPs' perceptions in the phenomenographic analysis, which could make it one of the strongest influences on prescribing.

Only a few GPs (N = 3) considered patient diagnosis and clinical decision to be influential factors on antibiotics prescribing. GPs who highlighted these factors listed the diagnostic challenges they encountered when diagnosing patients with infection such as limited availability of rapid diagnostic testing, the time gap between performing the test and obtaining the results and the lack of laboratory facilities within GP surgeries. In situations where there is a degree of uncertainty owing to a lack of a reliable test as in the case of the urine dipstick, delay in receiving laboratory results and having demanding patients or family members, the GP can develop a low-threshold and over-prescribe antibiotics either unnecessarily or inappropriately. Rapid and effective diagnostic techniques are required for diagnosis of infectious diseases to reduce uncertainty and promote more prudent antibiotics prescribing, as is evident by a cluster RCT aimed at assessing the effect of rapid and point-of-care testing for LRTIs on GPs' antibiotics prescribing, which showed prescribing of antibiotics to 31% of patients in a test group compared with 53% in the no test group ($p = 0.02$) (Cals *et al.* 2009). The finding in this study is consistent with several studies considering diagnosis from different angles as a factor that can influence GPs' antibiotics prescribing (Bjornsdottir and Hansen 2002, Petursson 2005, Kotwani *et al.* 2010, Vazquez-Lago *et al.* 2012, Teixeira Rodrigues *et al.* 2013), all of which linked diagnosis and clinical decision with misuse of antibiotics, especially when there is room for uncertainty or when there is a lack of diagnostic facilities and rapid diagnostic tests with high reliability. This factor was also described in the phenomenographic analysis study by GPs as one of the dimensions in different categories that can influence their prescribing views and perceptions.

One GP (N = 1) highlighted the role of ethos and ethical values in influencing GPs' antibiotics prescribing. The GP felt that she had a moral and ethical obligation when prescribing antibiotics to provide proper patient education and justification to avoid any negative consequences of unjustified prescribing. The finding was in line with the findings from a multi-country European qualitative study that investigated the factors influencing primary care doctors prescribing for LRTIs, which were that ethos is part of doctors' characters and can influence their antibiotics prescribing practice (Brookes-Howell *et al.* 2012). Furthermore, Brookes *et al.* (2012) found that clinicians who did not adopt a receptive ethos behaviour will continue to prescribe antibiotics as they have always done through routine and everyday experience even if it is inappropriate or against guidelines. Therefore, interventions are needed to change GPs' perceptions, to make them more receptive so that they can keep an open mind and embrace new developments to improve antibiotics prescribing and reduce resistance.

#### 5.4.1.2 Extrinsic Factors

Antibiotics prescribing was also found to be influenced by extrinsic factors related to GPs' interaction with patients. Patient-related factors can have a huge impact on antibiotics prescribing, whether they encourage GPs to prescribe, discourage them, or influence the choice of drug. Patients' characteristics were addressed by two GPs (N = 2) who indicated that both age and gender can be seen as important components that contribute to this factor. With some infections such as UTIs, age and gender are very important determinants of infection incidence (Foxman 2010). The finding in this study about age as a factor was in agreement with the finding of Teixeira Rodrigues *et al.* (2013), which indicated that patient's age can be a major determinant in antibiotics prescribing. In this research, linking the findings from the thematic and phenomenographic analyses suggested that patient's age can be a predictor for low-threshold prescribing in elderly patients whereas gender can be a predictor for the use of broad-spectrum antibiotics in male elderly patients.

Another extrinsic factor that dictated several of the GPs' antibiotics prescribing was patients' medical history and clinical characteristics (N = 8). This encompasses a variety of factors such as previous medical history, clinical presentation, that is, signs and symptoms, co-morbidities, frailty and severity of infection. GPs who acknowledged this factor highlighted the importance of considering patients' clinical situation before issuing prescriptions as these factors may interfere, modify or influence the decision to treat with antibiotics in terms of the choice of antibiotic, the dose, the frequency or the formulation (Leekha *et al.* 2011). In some situations, this factor might result in prescribing antibiotics that are not recommended as first-line therapy. For instance, it would be unsafe to prescribe for a patient with a known antibiotic allergy. Similarly, a previous history of recent antibiotic administration might mean an alternate antibiotic choice is required. In this study, only two GPs addressed patients' characteristics and medical history as factors that should be highlighted when a patient is elderly. Further, they recognised that factors such as severe clinical presentations, co-morbidities and frailty make them tend to prescribe an antibiotic very early for elderly patients (Herring and Williamson 2007). Overall, the findings in this study with regard to adults were in agreement with the findings of Teixeira Rodrigues *et al.* (2013). They showed a direct relationship between antibiotics prescribing and signs and symptoms, as described in 12 cases as well as co-morbidities, which were reported in four cases. However, patients' signs and symptoms were suggested to have the higher impact compared with co-morbidities on GPs' antibiotics prescribing. Findings from this study are also supported by the phenomenographic analysis, which included patients' clinical characteristics in different dimensions.

Two GPs saw patients' social situations and living conditions as an influential factor in both adult and elderly patients. they reported that knowing a patient's living status might encourage prescribing, discourage prescribing or influence the choice of antibiotic, particularly for elderly patients. Living alone can influence antibiotic administration especially if the antibiotic needs to be administered four times daily as in the case of nitrofurantoin, as one GP stated. This may place a burden on healthcare resources and family members. Additionally, elderly patients might have issues with memory and confusion, so a family member or carer might need to provide support to ensure that the antibiotic is taken at the right time for the right duration. In some situations, this factor might result in prescribing an antibiotic that is not recommended as first-line therapy. The finding regarding this social factor was consistent with the finding from the systematic review by Teixeira Rodrigues *et al.* (2013), who identified this factor as having a direct influence on GPs' antibiotics prescribing. The influence of this factor on GPs' prescribing was also clear in the phenomenographic analysis as being one of the dimensions that influence GPs' prescribing views.

Few GPs (N = 3) reported that patients' education level and lack of knowledge and understanding of the difference between viral and bacterial infections and the role antibiotics play in combating infection can influence GPs' prescribing patterns. The factor is important, though, because it is a significant determinant of antibiotics misuse and inappropriate use, as was evident from a cross-sectional study of 375 adult patients conducted using a pre-tested and structured questionnaire aimed at understanding patients' knowledge of antibiotics usage. It found that patients with good knowledge of the difference between viral and bacterial infections and a higher education level (university) had a better attitude towards rational antibiotics use than those with a lower education level ($p < 0.001$) (Abu Taha *et al.* 2016). When patients understand how antibiotics work it can cut down the demand and pressure exerted on GPs to prescribe antibiotics unnecessarily or inappropriately. Patients with poor knowledge, understanding or misconceptions about antibiotics often engage GPs in lengthy conversations, are confrontational and overwhelm healthcare resources by scheduling unnecessary appointments just to demand antibiotics, as stated by some GPs. The GPs interviewed valued elderly patients' previous experience with UTIs as it enabled them to recognise the symptoms and understand the consequences of untreated conditions, which in turn can encourage them to seek medical care early. The GPs understood that getting information can be more difficult for elderly patients as often they do not have easy access to the Internet, for instance, as most adults do. This factor was reported in a qualitative study by Hawkings *et al.* (2007), who carried out qualitative grounded-theory interviews with 46 adults to examine their attitudes towards and knowledge of AMR. The impact of patients' knowledge and understanding of infection, resistance and antibiotic activity was reported to be minimal in this study, possibly because the public perceive the problem of AMR to be beyond their influence. A pilot survey investigated 38 elderly participants' knowledge of antibiotic use, expectations regarding the prescription of antibiotics and awareness of AMR and showed that 66% (N = 25) were familiar with AMR and that 90% (N = 34) felt that it was an important healthcare issue. Further, 56% (N = 21) got their information from the media and 17% (N = 6) through their primary care physician. Moreover, 26% (N = 10) believed that antibiotics would help them recover from a common cold and 50% (N = 19) expected to receive antibiotics if they visited their primary care physician. These results illustrate the lack of knowledge held by elders regarding appropriate use of antibiotics owing to lack of primary care physicians' educational role (Mahmood *et al.* 2009).

Only one GP considered the desire for a quick fix to be a factor that influences antibiotics prescribing. Pressure to treat the UTI quickly was said to come from patients, family members or carers, often to be clear of infection in time for an exam, a special occasion or some other event such as a holiday. Thus, GPs who are aware of the quick fix issue might just issue an antibiotic prescription to end the consultation. This practice by GPs might not be possible to modify owing to time pressures and long waiting lists. The finding from this study was in line with the findings from Bjornsdottir and Hansen (2002), Kotwani *et al.* (2010) and Teixeira Rodrigues *et al.* (2013), who acknowledged the direct impact of patients' desire for a quick fix on GPs' antibiotics prescribing. Although this factor might be seen as a socially important influence for prescribing, GPs must base their decision on patients' ability to access healthcare facilities when needed if the GP decides not to prescribe.

Patient autonomy was found to be influential in antibiotics prescribing. This factor was highlighted by just a few GPs (N = 3) who addressed it only when they compared elderly patients with UTIs with adults. Although GPs have a moral obligation to respect patient autonomy (Stiggelbout *et al.* 2004, Littmann and Viens 2015), this was not the case when GPs were asked about the factors that might influence their prescribing for elderly patients with UTIs. They considered that elderly patients are usually less willing to be involved in the decision-making process, preferring GPs to decide for them. They suggested that this was because of the culture and time in which elderly people grew up, when patient autonomy was not discussed or explored extensively. This factor possibly drives some GPs to adopt low-threshold prescribing behaviour for elderly patients because they will take them seriously when they visit the surgery as a result of being less complaining as a group of patients, less likely to interfere in the GP's decision and less likely to demand an antibiotic. Bjornsdottir and Hansen (2002) linked GPs' prescribing tendencies with patients' complaint levels. This finding was not discussed in any previous qualitative research, which makes it a novel finding. Further research is indicated to explore the influence of elderly patients' autonomy on GPs' perceptions and decision to prescribe antibiotics.

### 5.4.2 Meso-Level Factors

GPs discussed four factors relevant to prescribing practice within surgery and local CCG contexts, that is, meso-related factors. The first was visits and education by advisors, which was seen by two GPs (N = 2) only. GPs who identified this factor acknowledged and valued the role of these advisors in influencing and reducing irrational antibiotics prescribing by GPs. According to GPs, they achieve this through executing external pressures, flagging GPs who prescribe irrationally and conducting regular visits and educational sessions to avoid antibiotics over-prescribing. The findings from this study support those of Kumar *et al.* (2003), who conducted grounded-theory interviews with 40 GPs to understand why they prescribe antibiotics for some cases of sore throat and to explore the factors that influence their prescribing. The results also support Wood *et al.* (2007), who interviewed 40 GPs to explore the reasons for their choice of prescribed antibiotics and both found and categorised the role of prescribing advisors among the strongest factors that can influence GPs' antibiotics prescribing behaviour. However, GPs must not depend heavily on prescribing advisors to guide and change their antibiotic prescribing behaviour as there is a shortage in the number of antimicrobial pharmacists advisors, as reported by one survey aimed at assessing the implementation of antimicrobial stewardship interventions in primary and secondary care. That survey, of 82 CCGs, found that only 5% (N = 4) of CCGs had antimicrobial pharmacists specialists working as advisors. This role was otherwise undertaken by quality or nursing clinical leads (N = 5; 6%) or by general practice clinical leads (N = 2; 2%) (Ashiru-Oredope *et al.* 2016). Therefore, increasing the number of prescribing advisors should be part of any antimicrobial stewardship interventions owing to their value and impact.

Auditing, monitoring and feedback seemed to be one of the strongest influences on GPs' antibiotics prescribing, as discussed by several GPs (N = 5). In the current study, the GPs identified the influence of auditing and feedback through activities by prescribing advisors and medicine management teams relating to both prescribing practice and cost control. The findings from this study were found to be consistent with those from a qualitative grounded-theory interview study by Wood *et al.* (2007) in the UK. Their study explored the reasons for 40 GPs' prescribing choices of antibiotics and found that auditing was one of the strongest factors that influence GPs' prescribing and choice, although it was not universally valued by all GPs interviewed. That said, audit and feedback should be part of any antimicrobial stewardship intervention owing to their value and impact in encouraging behaviour change (Eccles *et al.* 2007). This is supported by a recently published national RCT in the UK aimed at reducing unnecessary antibiotics prescriptions by GPs through feedback letter. Antibiotics prescribing was reduced by an average of 3.3% over a six-month period, saving over £92,000 in prescription costs (Hallsworth *et al.* 2016).

Secondary care prescribing behaviour appears to be another factor in this category that might influence GPs' antibiotics prescribing (N = 1). In practice, GPs respect hospital doctors professionally owing to their expert knowledge and experience, as was highlighted by UK-based qualitative in-depth interviews of 12 GPs, 12 hospital doctors and four focus groups, each with four GPs and four hospital doctors, aimed at describing the relationship, identifying strengths and possible problems and considering ways of improving professional interaction between GPs and hospital doctors (Marshall and Phillips 1999). However, the prescribing practice of some hospital doctors can have unexpected impacts and influences on GPs' prescribing practice, which is not only annoying to GPs but can have negative consequences in the long term. The GP who highlighted this factor extensively indicated that there are two pathways of influence. The first relates to GPs who prescribe antibiotics but find the outcome poor, ineffective or associated with side effects or interactions. They then seek advice from local hospital consultants who might not adhere to local or national recommendations, preferring to prescribe based on their experience. This can lead GPs to adopt the same prescribing practice. The second pathway concerns patients who are discharged from hospital, attend an outpatient clinic or have been treated by a consultant who works in a hospital and whose practice is based totally on hospital experience. The consultants prescribe according to common hospital practice, which leads patients to demand the same antibiotic next time they visit their GP, regardless of whether it is suitable for their particular infection in a community setting. This finding supports Kuehlein *et al.* (2011), who studied the influence of secondary care doctors on GPs' antibiotics prescribing and perceptions. Another GPs' prescription analysis study in the UK by Taylor and Bond (1991) identified that 1,092 (17.6%) GPs out of 6,195 mentioned hospital doctors as being major influences on prescribing habits and perceptions of some drugs including antibiotics (Taylor and Bond 1991). Thus, hospital doctors should be careful when advising their colleagues from primary care or treating patients in GP surgeries to avoid the spread of hospital practice that could indirectly promote inappropriate antibiotics prescribing.

Implementation of local policies, guidance and formulary was discussed as another factor that can influence GPs' (N = 9) prescribing on the meso-level. GPs in this study described how antibiotics prescribing is strongly influenced by adopting surgery and local practice policies and guidance, although some of these local policies and guidance might be restrictive in nature or irrelevant to primary care settings because they were based on data obtained from local hospitals, which might not always translate well to GP surgeries, as highlighted by some GPs. Although this was seen as one of the factors impacting on prescribing, the GPs admitted to sometimes finding themselves forced to step outside these policies and guidance to better serve an individual patient. Moreover, some GPs were cynical about the possible cost-saving incentives behind such guidance. Overall, GPs valued the role of local guidance and local policies on their antibiotics prescribing. This was in line with Kumar *et al.* (2003), who referred to local policy as one of the factors that influences all GPs' prescribing with regard to decision-making, and partly in line with Teixeira Rodrigues *et al.* (2013), whose results were inconclusive. However, this inconclusive finding can be explained by including studies from other non-primary care settings such as surgical wards and emergency departments.

### 5.4.3 Macro-Level Factors

GPs discussed a number of factors that went beyond the previous level to include society and national healthcare system contexts at the macro-level. This category consisted of 10 factors that the interviewed GPs considered were major determinants of antibiotics prescribing practice.

Limited consultation time was stated by two GPs (N = 2) as a factor that influences GPs' antibiotics prescribing. In average, GPs have a 10–15 minute time slot for each patient (Lakhani *et al.* 2007). This restrictive time allocation in addition to other pressures such as long waiting lists might result in GPs issuing prescriptions against their better judgement. GPs reported a consultation time of 10–20 minutes per patient. Elderly patients with co-morbidities complaining of infection might need to extend this time. The GPs who addressed this factor considered the benefits of having more time to be able to make informed decisions by taking proper histories and carrying out more investigations as well as having the opportunity to explain more about antibiotics to patients, especially when the decision has been made not to prescribe despite the patient's expectations. The findings corroborate those of previous studies (Bjornsdottir and Hansen 2002, Petursson 2005, Kotwani *et al.* 2010, Teixeira Rodrigues *et al.* 2013), all of which addressed the influence of time pressure, which can lead GPs to exhibit low-threshold tolerance, especially when it is linked with heavy workloads and a shortage in the GP workforce. Issuing a prescription becomes the quickest option and a way of coping.

Many of the interviewed GPs (N = 11) stated that national guidelines and evidence can have a strong impact on antibiotics prescribing practice. GPs are responsible for ensuring that what is prescribed is supported by evidence and literature. In the phenomenographic analysis of this research, the GPs showed varied levels of knowledge and awareness regarding UTI guidelines while in the thematic analysis they described the strong impact of guidelines on the decision to prescribe antibiotics, especially if the guidelines and evidence were issued by national bodies and organisations such as NICE, DoH and PHE and are up to date. However, being aware of and familiar with guidelines and evidence does not guarantee their uptake, as reported by Cabana *et al.* (1999), Carlsen *et al.* (2007) and Casey (2013), who referred to several factors such as lack of confidence in developers, disagreement between the theoretical content of guidelines and daily practice, and organisational constraints. Stepping outside recommendations might not always be wrong as guidelines have been known to be rigid and not suitable to adopt for many patients for reasons such as existence of co-morbidities and poor compliance (Woolf *et al.* 1999). Additionally, some GPs might feel that guidelines can interfere with their prescribing autonomy, therefore they prefer not to conform with them (Woolf *et al.* 1999). Since this factor has a strong influence on prescribing practice, as highlighted by the majority of GPs, healthcare bodies and organisations must synthesise their guidelines and evidence to be more user friendly, concise, flexible and representative, and to encourage uptake and assimilation into practice. Tonkin-Crine *et al.* (2013) qualitative interview study of 50 participants from five countries including the UK supports this. Moreover, guidelines and evidence can be useful tools in disseminating key messages to encourage macro-level changes in antibiotics prescribing attitudes. Much of the literature debates the influence of guidelines and evidence on antibiotics prescribing in settings other than primary care. However, the findings in the current study support those of Kotwani *et al.* (2010), Vazquez-Lago *et al.* (2012), Teixeira Rodrigues *et al.* (2013) and Duane *et al.* (2016), who agreed on the direct impact of guidelines on GPs' antibiotics prescribing. Interestingly, some GPs from Petursson (2005) study saw guidelines as a threat in practising medicine and were unwilling to conform with antibiotics guidelines. GPs who do not comply with antibiotics guidelines might tend to prescribe antibiotics more frequently, unnecessarily or inappropriately.

Shortage of antibiotics was addressed as a factor influencing antibiotics prescribing practice by several GPs (N = 7). In this study GPs reported antibiotics shortages lasting for several weeks for some antibiotics. From a marketing perspective, antibiotics were reported to be removed from the market six times faster than new ones were being produced (Reinberg 2015). Occasional antibiotics shortages might be a consequence of things such as manufacturer mergers, quality issues, supply and procurement problems of pharmaceutical companies, facility consolidation, narrow profit margins and internal purchasing issues within the healthcare system, as stated by the GPs. Shortages might have significant implications in the context of other factors that limit availability of effective antibiotics, including a shrinking pipeline of new antibiotics and increasing drug resistance (Simpson *et al.* 2009). By itself, a shortage can influence GPs' antibiotics prescribing by limiting their choice of drugs and exposing patients to risks, especially in the case of drug-resistance infection or lack of alternative antibiotics. If GPs continue to prescribe antibiotics inappropriately under the influence of some of the previously discussed factors, antibiotics shortages might continue to rise in the coming years, which might impact patients' clinical outcomes. No previous studies have discussed antibiotics shortages as one of the influencing factors on GPs' antibiotics prescribing practice. Further research is indicated to explore the influence of antibiotics shortage on GPs' inappropriate antibiotics prescribing.

Incentives were seen by a couple of GPs (N = 2) as a factor that might affect antibiotics prescribing practice. In the current study, the two GPs who referred to this factor in adults both discussed the economic side of it and one linked incentives to prescribing quality. Taking part in antibiotics incentive schemes was found to influence GPs' prescribing behaviour, in this case relating to the choice of antibiotic, improved antibiotics prescribing and reduced prescribing cost by keeping it within the annual indicative prescribing budget (McNulty and Francis 2010). This influence was clear in a cross-sectional survey in the UK that examined the prescribing incentive schemes used by 121 primary care groups and found that the most frequently used clinical areas for prescribing indicators were antibiotics in 76% (N = 92) of cases with the majority resulting in desired changes in antibiotics cost savings and improved prescribing quality perception with, to a lesser extent, improvement in prescribing short courses and according to guidelines (Ashworth *et al.* 2002). Only two previous qualitative studies have highlighted the direct influence of healthcare system incentive schemes on antibiotics prescribing (Petursson 2005, Wood *et al.* 2007). The concept of incentive in Petursson's (2005) study was found to encourage prescribing behaviour, which in turn can lead to promotion of inappropriate prescribing and increase AMR. In Wood *et al* (2007), incentive was described to be a strong influence on the choice of antibiotic but not on prescribing. Therefore, antibiotic incentive schemes must be linked with judicious prescribing in complying with recommendations.

The influence of the media, whether in the form of TV, radio, the Internet or newspapers, was considered one of the macro-level factors by five GPs interviewed. GPs who supported this factor considered the media to be a very powerful communication tool that can shape patients' and the public's views by evoking reactions to podcasts, published stories, news and medical insight, whether negatively through causing downward prescribing trends or positively. The role and impact of the media on the public and infection was described in qualitative research to explore the attitudes of the public towards bacterial resistance (Hawkings *et al.* 2007). They interviewed 46 members of the public and found the media to be the main information source on bacterial resistance.

However, media content might be misleading or written in a way to attract attention, which may counteract and complicate the work of many GPs. The GPs in this study revealed that the media might be responsible for influencing patients' and society's demands for and expectations of antibiotics, either towards prescribing or in terms of reassuring patients about their conditions. Patients who are influenced negatively by the media can be seen as a challenge for GPs as their expectations and demands might evoke stress and frustration for GPs during consultations. Perhaps healthcare bodies should work closely with media sources to ensure that proper content is handled more evenly and accurately, as highlighted by a report published by (WHO 2012b). In addition, key messages need to be delivered to the public on behalf of GPs including educational programmes for different ages aimed at explaining the differences between viral and bacterial infections, activity of antibiotics in bacterial infections, when to seek medical attention for antibiotics, threat of resistance and the public role and responsibilities in this regard, the importance of reducing demand for antibiotics if not indicated and when to discuss expectations with GPs. Surprisingly, no previous qualitative works have identified the influence of the media on antibiotics prescribing behaviour by GPs. Further research is indicated to explore the impact of the media on antibiotics prescribing in the community.

In the current study, two findings were associated with the financial impact on prescribing and services provided by healthcare bodies. The majority of GPs acknowledged the impact of antibiotics cost (N = 8) and healthcare resources and constraints (N= 2) on prescribing practice. GPs who addressed cost as an influencing factor said that it should not be a major determinant for prescribing. In this study, antibiotics cost was viewed from two different perspectives: acquisition cost, that is, purchase cost, and cost-effectiveness. In the UK, the NHS equates good prescribing with the lowest-cost prescribing that meets public health needs (Duerden *et al.* 2011). Moreover, the NHS strongly recommends that GPs keep their prescribing costs to a minimum as well as prescribing generically where appropriate (Duerden *et al.* 2011). Most antibiotics are now off patent, which has made them cheaper owing to the availability of several generic preparations. However, the existence of these might encourage some GPs to prescribe antibiotics more frequently. GPs who focused their discussion on acquisition cost fell into two camps: one group respected the economic value of antibiotics in general whereas the second group underestimated the economic value of antibiotics, considering it to be only a minor factor. Most GPs who were consciously aware of cost-effectiveness as a factor believed that the

NHS pressurises GPs to adopt a cost-saving approach rather than a cost-effective one when prescribing. Adopting cost-effective prescribing might promote more rational prescribing but at the same time increase expenditure, which might be against healthcare policies. Some GPs highlighted the impact of limited healthcare resources and funds on antibiotics prescribing behaviour. GPs are disciplined to make efficient use of healthcare resources, yet the NHS resources available are under pressure because of increasing costs, limited scope for productivity gains and constrained public resources (Dawda *et al.* 2010). With all these constraints such as limited healthcare budget, GPs might find themselves in a challenging position with regard to antibiotics prescribing. Constraints as a factor can put pressure on GPs, which can be reflected negatively in the quality of prescribing decisions or positively by directing and encouraging rational and cost-effective prescribing. Thanks to financial constraints, GPs have the dilemma of trying to prescribe both rationally and cost-effectively, putting them under increasing pressure from the demands of more consumerist patients. The finding regarding cost supports those of Bjorkman *et al.* (2013) and Teixeira Rodrigues *et al.* (2013), who linked the concept of antibiotics' low cost with the tendency of antibiotics prescribing. Owing to the low cost of antibiotics compared to the cost resulting from non-treatment hospitalisation, GPs might prefer to prescribe antibiotics on the basis of 'just in case' more frequently and unnecessarily to prevent disease progression. Therefore, healthcare organisation should promote cost-effective prescribing rather than cost-saving. Limited healthcare resources and constraints were not previously discussed by any qualitative research related to antibiotics, making this finding novel. Further research is indicated to explore the impact of healthcare resources constraints on GPs' antibiotics prescribing practice.

Pharmaceutical companies can play an important role in encouraging prescribing through several methods such as arranging sponsored events, visiting surgeries to give GPs marketing speeches and distributing personal gifts, gifts for the surgeries and free samples to promote and sell their products (McNulty 2001). In this study one GP (N = 1) valued these presentations and activities as they give him convenient, up-to-date information in addition to time to socialise with peers. However, the GP understood that pharmaceutical companies might provide biased or selected information about products including antibiotics, as one mixed methods study of 107 UK GPs concluded (Prosser *et al.* 2003). In this study, the influence was seen to be minimal, as highlighted by one GP who felt it might be because of the lack of new antibiotics or classes of antibiotics being produced. The influence of pharmaceutical companies on antibiotics prescribing was reported in

Kotwani *et al.* (2010), Vazquez-Lago *et al.* (2012) and Teixeira Rodrigues *et al*. (2013), who found pharmaceutical companies to be more influential in terms of antibiotics prescribing because of their direct relationship. Although this influence might be minimal, it should not be ignored in any strategy aiming for prudent antibiotics prescribing.

Unsafe and unnecessary over-prescribing of antibiotics was also identified by two GPs (N = 2) as a factor that can impact antibiotics prescribing practice. Although antibiotic use can be beneficial to individuals, excessive use can be detrimental (Laxminarayan *et al.* 2013). Prescribing more antibiotics than are clinically needed was linked with negative consequences such as increased antibiotic resistance, unnecessary costs, side effects, rendering antibiotics ineffective (Llor and Bjerrum 2014) and encouraging patients to believe they need antibiotics even for trivial conditions – ‘a pill for every ill’, as was highlighted in one governmental report (SMAC 1998) aimed at examining the issue of AMR in relation to clinical prescribing practice in the UK. In this study, one GP’s perspective was concerned with the negative consequences of over-prescribing in relation to microbial resistance and side effects whereas the second GP had linked over-prescribing behaviour with visits from prescribing advisors, suggesting that their monitoring and feedback can have a positive impact on GPs’ future prescribing to cut down this behaviour. This diversity of the perspectives within the same factor could explain the variations among GPs’ antibiotics prescribing. Surprisingly, no previous qualitative works have identified over-prescribing as a factor that can influence GPs’ antibiotics prescribing practice. Further research is indicated to explore GPs characteristics and the reasons for their antibiotics over-prescribing behaviour.

Antibiotics prescribing is not limited to GP surgeries and hospitals; it is also a societal matter because it involves public attitudes and beliefs. The impact of society and public expectations on antibiotics prescribing was mentioned by some GPs (N = 5). Society’s desires and expectations can be very complex since they concern the behaviours that people who live within society are expected to sustain. Because these behaviours are a result of interactions between people, GPs and the healthcare system, society’s influence on antibiotics prescribing can be seen in the form of societal demand to reduce the disease burden and infection transmission (McDonnell Norms Group 2008). Society’s views must be shifted towards a sustainable rise in antibiotics awareness and limiting unnecessary use to preserve the value of antibiotics for future generations. Cutting down

GPs' non-pharmacological prescribing in addition to balancing individual and societal interests may be required. However, this view related to elderly patients with UTIs is not the same as for adult patients with UTIs. GPs, society and even elderly people are greatly aware that elderly patients need antibiotics for UTIs more than other age groups. This might explain why GPs have a lower threshold for prescribing antibiotics for elderly patients with UTIs. This view can be related to an ageist attitude within society. Interestingly, the finding has not been explored by any previous qualitative study, which makes it a novel finding.

In this study, only two GPs considered the factors influencing antibiotics prescribing in elderly patients with UTIs to be the same as for adult patients with UTIs on all three levels. The GPs who were aware of variations between elderly and adult patients' physiology, co-morbidities and other related factors still considered the factors the same. Moreover, those GPs considered the influence of local policy and the needs of society to be the driving forces that made them consider adult and elderly patients the same. Therefore, to enforce changes in GPs' antibiotics prescribing for elderly patients, interventions must consider the influence of society and local policies in their design for effective behaviour change.

The findings from the thematic analysis with regard to demographics revealed that females were associated with the following factors when discussing adult patients: fear (N = 1), diagnosis and clinical decision-making (N = 3), ethos and values (N = 1), desire for a quick fix (N = 1), influence of secondary care doctor practice (N = 1), time pressure (N = 2), responsibilities of other HCPs (N = 1); and fear (N = 1) and no differences between adults and the elderly (N = 2) when discussing elderly patients. The influence of pharmaceutical companies and industry was the only factor associated with males (N = 1). Moving to GPs' age, factors including: diagnosis and clinical decision-making, ethos and values and time pressure in adults and fear and patient's level of understanding and knowledge in the elderly were highlighted by GPs who were 40 years and younger (N = 10). Pharmaceutical companies as a factor was highlighted by a GP aged 45 (N = 1). With regard to GPs' years of practice, no direct relationship to the factors was observed. Owing to the small number of GPs participating in this research, it was difficult to establish a concrete relationship between the factors influencing GPs' prescribing and GPs' demographics. Although there might be an association between age and certain factors, as highlighted above, this could be justified by the relatively high number of young GPs included in the research compared with other ages. This finding with regard to age, gender and years of practice is supported by a qualitative systematic review and another quantitative systematic review about the factors influencing GPs' antibiotic prescribing Lopez-Vazquez *et al.* (2012) and Teixeira Rodrigues *et al.* (2013), which could not establish a solid relationship between these factors and GPs' demographics. A recently published three-year cohort study in Portugal that included 1,094 primary care physicians and aimed to assess the influence of the determinants of physicians' prescribing on the quality of antibiotic use showed no statistical difference with regard to age (OR [95% CI] = 0.99 [0.95–1.03]; $p = 0.105$) or gender and contradictory results for previous clinical practice, years of practice and CME (Teixeira Rodrigues *et al.* 2016). An ethnographic qualitative study might be indicated to explore the influence of GPs' demographics and years of practice on their prescribing practice.

## 5.5 Summary

In summary, this chapter presented the key findings for qualitative studies related to GPs' antibiotics prescribing for elderly patients with UTIs. The outcomes of the phenomenographic analysis were presented in the form of categories of description and outcome space. In this study, five qualitatively distinctive categories of description were identified; namely, perceptions, knowledge, decision, practice and approach. The internal horizon of GPs' perceptions on antibiotics prescribing comprises multiple foci that include healthcare, diagnostics and investigation, diseases, drugs, economics, GPs, patients, gender and society; whereas the external horizon consists of training, education, peers, patients, the healthcare system, personal experience and guidelines. Categories of description were displayed in an outcome space to show the complex structure of the phenomenon of antibiotics prescribing as experienced by GPs.

The findings of the thematic analysis were presented in the form of themes as well as quotes from participants' interviews. Themes were grouped into one of three main categories: micro, meso- and macro-level related factors. Micro-level related to factors that target GP–patient interaction; meso-level related to factors were mainly relevant to practice and the CCG context; and macro-level related factors provided the wider picture of factors that take into account society and healthcare resources. Additionally, factors that influenced GPs' prescribing for elderly patients with UTIs were seen from two different standpoints. The first standpoint was addressed by participants who recognised elderly patients as a distinctive group of the population in some aspects of antibiotics prescribing, if not all. As a result, specific factors were seen to be important and influential in terms of antibiotics prescribing. The second standpoint was highlighted by a group of participants who looked at elderly patients with UTIs as a subgroup of adults and therefore saw no differences in terms of factors that influence antibiotics prescribing for UTIs.

# Chapter 6 Overall Discussion and Conclusion

## 6.1 Introduction

In this final chapter, summary of research key findings, overall discussion and conclusions drawn from this research are offered, followed by a section addressing the original contribution of this research to the body of knowledge, research methodology and theoretical contribution. The chapter concludes by offering suggestions for further research.

## 6.2 Summary of Research Key Results and Findings

- The research suggests high prevalence of UTIs in elderly female patients compared with elderly male patients.
- Adherence results showed that some GPs' prescribing was not in line with the available good practice points as they prescribed broad-spectrum antibiotics and issued prescriptions with durations other than those recommended either for treatment or for prophylaxis.
- The research identified five distinct categories of description representing the ways in which GPs perceive antibiotics prescribing in elderly patients with UTIs; namely, perceptions, knowledge, decision, practice and approach.
- GPs' knowledge and perceptions about antibiotics were found to be shaped through seven external horizons: undergraduate education, postgraduate training, personal experience, interaction with peers, interaction and influence of patients' expectations, the healthcare system, and availability of guidelines and evidence.
- The research identified 29 factors that may influence GPs' antibiotics prescribing for UTIs. These factors comprise GP-related factors, patient-related factors and healthcare system-related factors and were found to influence GPs' antibiotics prescribing in patients with UTIs across prescribing practice at the micro-, meso- and macro-level.

## 6.3 Overall Discussion

Prior to the commencement of this research, a number of gaps were identified from the reviewed literature and bibliographies in the existing knowledge of GPs' antibiotics prescribing for elderly patients with UTIs in the UK, gaps this thesis has sought to address. Overall, the aims and research questions in Chapter Two have been achieved through a mixed methods research approach. One part of this thesis investigated the prevalence of UTIs in elderly patients, antibiotics prescribing by GPs for elderly patients with UTIs and audited GPs prescribing against available recommendations through a special type of pharmacoepidemiological study, namely, a DUR using the IMS-DA database. Another part in the form of phenomenographic qualitative research explored GPs' views and perceptions about antibiotics for elderly patients with UTIs as well as factors that can influence GPs' antibiotics prescribing practice for adult and elderly patients with UTIs. The following section discusses the key findings from this research.

Overall, UTIs were found to be a more common health condition in female elderly patients than in male elderly patients, which might be owing to gender-related factors such as the anatomical structure of the female urethra, increased incidence of urinary incontinence, previous and recurrent history of UTIs, presence of DM, low oestrogen levels as well as longer life expectancy in females compared with males (Moore and Spence 2014). The prevalence of UTIs increased with advancing age in the elderly patients studied until the age of 93, when it started to decrease. Almost 49% (N = 37,815) of the elderly patients who visited GP surgeries for UTIs have received at least one antibiotic. From a drugs perspective, trimethoprim was among the most commonly prescribed antibiotics for elderly patients with 15,772 (41.7%) prescriptions followed by nitrofurantoin (N = 9448, 25%). GPs' non-adherence to SAPG good practice points took place in practice in two different forms. The first form related to prescribing broad-spectrum antibiotics, namely, cephalexin, co-amoxiclav and ciprofloxacin in 9,125 (24.1%) of all UTI antibiotics prescriptions. The use of broad-spectrum antibiotics in elderly patients should be avoided since these drugs can increase the susceptibility of elderly people to *Clostridium difficile* infection (SIGN 2012, SAPG 2013). The second form of non-adherence was seen through prescribing antibiotics for durations other than those stated by the recommendations in 4,416 (28%) trimethoprim prescriptions as well as 4,771 (50.5%) of nitrofurantoin prescriptions, or in prescribing alternative antibiotics choices in particular for LUTIs. This practice could result in deterioration of elderly patients' conditions, expose them to ADRs and increase or develop bacterial resistance. Overall, the results from the comparison between GPs' prescribing practices and UTI recommendations suggested that there was a lack of adherence to recommendations, variations in antibiotics prescribing as well as inappropriate antibiotics prescribing in terms of antibiotic choice and duration of antibiotic therapy.

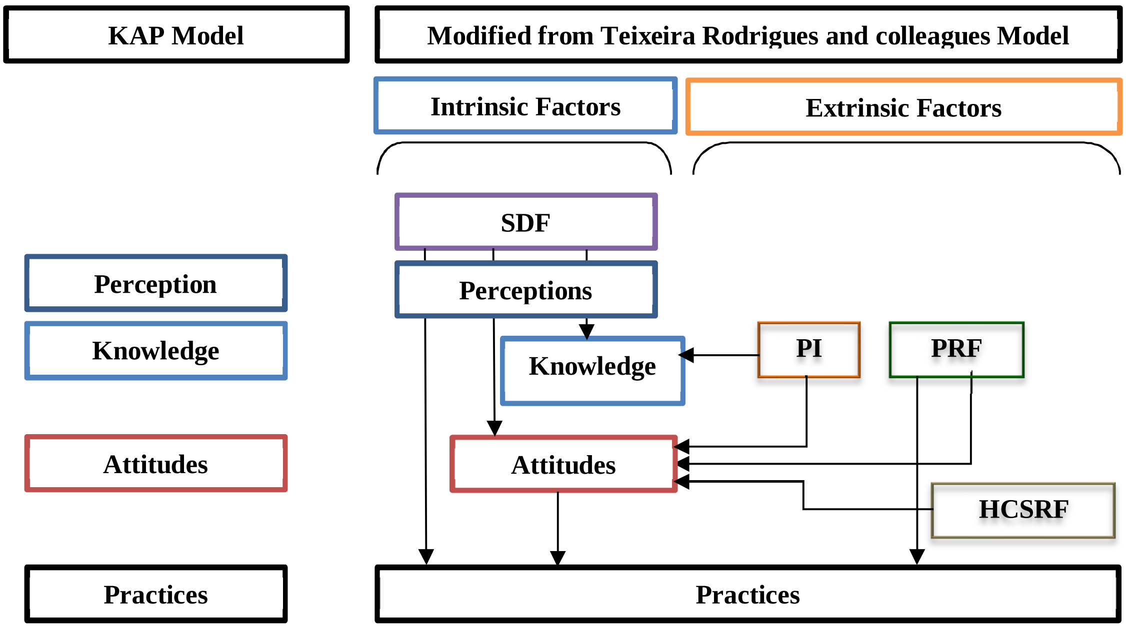
During the interviews, the GPs showed a high level of awareness of both diagnostic aspects of UTIs in elderly patients with regard to distinguishing between UTIs and ASB as well as prescribing aspects of antibiotics, namely, safety, practicability, compliance and quality of prescribing, relative to elderly patients. From a qualitative and phenomenographic perspective, the findings from all five categories – perceptions, knowledge, decision, practice and approach – clearly suggest the presence of substantial variations among GPs' views, which explain the way GPs prescribe and act. Furthermore, they demonstrate how the phenomenon of antibiotics prescribing by GPs for elderly patients with UTIs is complex and diverse, as was evident from the presence of several dimensions representing different views and conceptions among GPs. Overall, it is acceptable to see variations in perceptions within the same category. Individuals all have different life experiences, as highlighted in Chapter Three. However, the presence of contrasting perceptions within the same category in different dimensions might explain why there are variations in antibiotics prescribing practice among GPs, as was detected in the study. The presence of variations in antibiotics perceptions, knowledge, awareness of and familiarity with guidelines, decision to treat UTIs and approaching elderly patients collectively can explain why there was a lack of adherence to recommendations, variations in antibiotics prescribing as well as inappropriate antibiotics prescribing in terms of using broad-spectrum antibiotics and non-recommended antibiotic choices and therapy durations, as shown by the DUR study. Moreover, lack of awareness of and familiarity with any guidelines might suggest that there is a problem within the evidence dissemination process. The findings showed several shared dimensions across some categories, including patients' socio-medical status, antibiotic concerns, diagnostic tests, patients' safety and compliance, and the no variation dimension in approach or practice. However, the GPs' perspectives likely differed according to the nature of the specific question and the GPs' experience.

Additionally, the findings demonstrate how some GPs were more flexible when deciding to prescribe antibiotics for elderly patients with UTIs by showing low-threshold behaviour, considering age, severe illness or presentations, co-morbidities and frailty as predictors for. The camp of GPs who reported a modified treatment approach according to gender differences considered being male a predictor for using broader-spectrum antibiotics and prescribing longer or extended durations and/or alternative choices compared with elderly female patients. These two irrational prescribing behaviours could be a result of the influences of the external horizons that shaped GPs' antibiotics prescribing practice perceptions rather than the guidelines for this particular context including peers and GPs' personal experience.

The findings suggest that GPs' antibiotics prescribing for UTIs is influenced by numerous and diverse factors that make the prescribing process very complex. Factors highlighted by the GPs fell into three major contexts: micro, meso and macro and factors may operate at each level alone, or across all three, as in the cases of over-prescribing, guidelines, policies and resistance. Moreover, the findings revealed a lack of agreement among GPs on any factor in addition to variations in reporting factors that can influence prescribing practice in either adult or elderly patients. The findings suggest that a host of clinical as well as non-clinical factors can influence antibiotics prescribing. According to the number of factors, it seems that GPs are mainly influenced by micro-level factors followed by macro-level factors and then meso-level factors. In micro-level factors, both intrinsic and extrinsic factors received the same weight of importance among the interviewed GPs. Overall, 29 factors were cited as influencing GPs' antibiotics prescribing for adult patients with UTIs whereas 10 factors were named as determinants for antibiotics prescribing in elderly patients with UTIs. Of these, nine were shared between both age groups: complacency, fear, concerns about antibiotics, medical history and clinical characteristics, patients' social situation and living conditions, patients' level of understanding and knowledge, incentives, patients' autonomy and society. Gender and age were the only factors discussed in elderly but not adult patients. This might suggest that GPs have a better understanding of adults as patients compared with the elderly. Responses from GPs to questions related to the elderly were noticeably very short and hesitant compared with responses related to adult patients.

Certain factors in the thematic analysis also emerged from the phenomenographic analysis, including but not limited to social and medical status, concerns, guidelines, local guidance, resistance, diagnosis and clinical decision, training, education, society, healthcare systems, economics and gender. This finding from two different methods of analysis supports '*triangulation*'. Moreover, that the GPs' views placed them in two camps with regard to factors within elderly patients could also support the findings from the phenomenographic analysis with regard to variations in practice and approaches as well as explain the variations in prescribing from the DUR study. Furthermore, discussions with GPs revealed contradictory opinions with regard to certain factors seen from different perspectives or angles when comparing adults with the elderly. For instance, complacency, patient knowledge and previous experience with UTIs in elderly patients were seen as factors that can encourage GPs to prescribe antibiotics for elderly patients but not necessarily for adult patients. These can result in lack of adherence to recommendations, variations in antibiotics prescribing as well as inappropriate antibiotics prescribing in terms of antibiotic choice and duration of antibiotic therapy, which supports the findings from the DUR study with regard to prescribing.

The findings from the research explain what GPs do and do not see happening in relation to antibiotics prescribing for elderly patients. Therefore, a theoretical framework was proposed to model the GPs' knowledge, attitude, perceptions and practice to enable the development of multifaceted practical interventions. The one proposed was modified from the literature-based framework proposed by Teixeira Rodrigues *et al.* (2013) by incorporating perceptions emerged from the phenomenographic analysis and considering perceptions about antibiotics in terms of the intrinsic factors that were the most complex influence on GPs' antibiotics prescribing. The proposed theoretical framework integrates GPs' perceptions with other core components of the original KAP model and demonstrates how they work together in shaping GPs' practice (Figure 32).




**SDF: Sociodemographic factors**
**PI: Pharmaceutical industry**
**PRF: Patient related factors**
**HCSRF: Healthcare system related factors**

Figure 32: Modified theoretical framework from Teixeira Rodrigues framework of interrelationships among factors influencing antibiotics prescribing (Teixeira Rodrigues *et al.* 2013)

As there is little evidence about the factors that influence antibiotics prescribing in general, and for UTIs in elderly patients in particular, a finding that perhaps explains why the different interventions implemented to promote rational antibiotics prescribing have not been successful in meeting expectations was highlighted by (Lopez-Vazquez *et al.* 2012). To make this work, all identified factors from the three thematic analysis levels (macro, meso and micro) were considered in addition to GPs' views and perceptions identified from the phenomenographic analysis to design a successful multifaceted intervention approach (Figure 33). The effectiveness of this proposed multifaceted intervention can be enhanced and informed by utilising implementation science in form of theoretical domains framework (TDF) which was shown to be very useful in understanding the barriers to, and facilitators of, uptake of even the most "evidence based" intervention strategies. The TDF consists of 14 conceptual determinants and associated constructs from organisational and psychological theory that putatively influence behaviour and stimulate behaviour change (Lipworth *et al.* 2013).

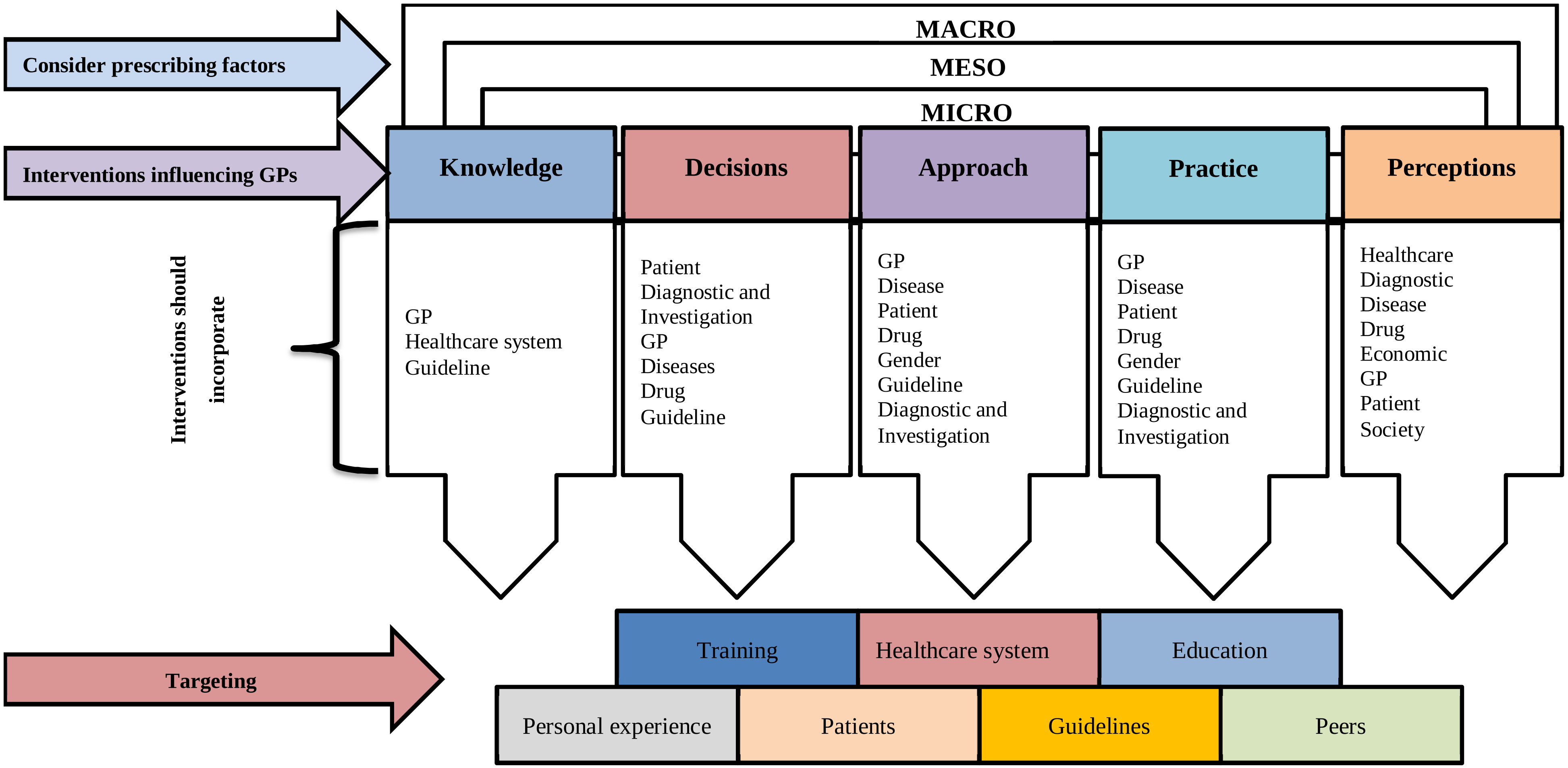



Figure 33: Proposed components of a multifaceted intervention incorporating the findings from the mixed methods research

## 6.4 Research Appraisal, Strengths and Limitations

Owing to the nature of the gaps identified by the literature review, which include UTI prevalence in the elderly, GPs' antibiotics prescribing adherence to good practice points for UTIs in elderly patients, GPs' antibiotics prescribing perceptions and views on UTIs in the elderly and factors influencing GPs' antibiotic prescribing for UTIs, the study used mixed methods research in the form of a DUR and a phenomenographic approach to explore GPs' antibiotics prescribing for UTIs in elderly patients in the UK. This research was one of the first of its kind in the UK. The use of mixed methods seemed well suited to the thesis aim and objectives. As was argued in Chapter Three, quantitative methods can provide invaluable information about the epidemiology of UTIs and the size of the problem of inappropriate antibiotics prescribing for elderly patients, but do not provide an in-depth view of GPs' behaviour in the same way that the qualitative approach taken here does. This research was unique in approach and intensity. Quality time was spent harvesting IMS-DA data and talking with GPs to investigate their prescribing practice. This allowed a better understanding of the UK's medical records databases, the general practice system, GPs' prescribing practice and the regulatory aspects of prescribing. The methods, sampling strategy, data analysis and in-depth presentation of the findings of this research have all been described in detail to allow others to adopt the research method or to assess the transferability of the findings.

### 6.4.1 Quantitative Study

The quantitative study took the form of a retrospective, observational, cross-sectional DUR. The reason for choosing this method and design was its known efficiency in addressing and describing prevalence, patterns, trends as well as exploring the adherence of GPs to the good practice points, that is, auditing (Wertheimer 1988, Dukes 1993). Furthermore, this study design could lead to planning for future interventions intended to improve prescribing behaviour in addition to being inexpensive, quick and easy to perform compared with other types of drug utilisation research, requiring only the use of routinely accessible data (Wertheimer 1988, Dukes 1993). The main disadvantages of this design were the limited number of variables available for analysis and there being more potential for bias and confounding than in other drug utilisation study designs. However, the bias and cofounding can be overcome by adhering to a well-structured study design (Cooke 1991, Shalini *et al.* 2010).

To serve the purpose of this study, data were obtained from the IMS-DA database. It was selected because it contains robust prescriptions data that were collected from a good number of GP surgeries and issued by GPs from different geographical distributions, which makes this database largely representative of the UK population and thus allows its results to be generalised (Becher *et al.* 2009). Moreover, the IMS-DA database is known for being valid, inexpensive and of high quality. It has robust quality control standards carried out by an IMS Health panel (Becher *et al.* 2009). Additionally, an IMS-DA access licence was available, which was a further advantage. These characteristics of the IMS-DA database allowed the retrieval and analysis of a massive amount of population-based data, which provided descriptive insight into UK GPs' antibiotics prescribing volume and the status of GPs' adherence to recommendations on a national level. In this study, more than 77,000 UTI events in elderly patients were obtained from 135 GP surgeries from England Scotland, Wales and Northern Ireland. The huge number of events is one of this study's strengths as it resulted in increasing the external validity of the results and ensuring that the results were representative of the elderly population in the UK. Moreover, the use of a computerised database to study routinely collected patient records made by trained GPs also minimised issues associated with the Hawthorne effect and recall bias, which can frequently be seen in any auditing research.

However, there were inherent limitations associated with this method that need to be addressed. First, it is important to mention that the data held within the IMS-DA database were collected primarily for clinical rather than for research purposes (Ogdie *et al.* 2012). Second, as with any computerised database, misclassification or imprecise use of the disease classification system might have occurred during GPs' data entry as in Ki *et al.* (2004), Galatti *et al.* (2006), Czaja *et al.* (2007), Laupland *et al.* (2007), Caljouw *et al.* (2011) and Marques *et al.* (2012), which in turn might have resulted in incomplete capture of all cases or measuring of GPs' adherence. For instance, the study found that most recorded UTI events were site unspecified, which made comparison between GPs' prescribing and the recommendations problematic. Although IMS-DA has quality control measures in place that help to improve the records, some inaccuracies may have remained. Third, lack of laboratory results including urine analysis, urine cultures and renal function tests in addition to availability of limited variables might have influenced the results of the study in several ways such as distinguishing between UTIs that require antibiotic therapy versus ASB that does not, and influencing GPs' antibiotic choice, dose or duration as in Kahan *et al.* (2005), Eriksson *et al.* (2010) and Haasum *et al.* (2013). However, the study assumed that elderly patients who were coded as having UTIs and given antibiotics had a high likelihood of actually having a UTI. Fourth, lack of patients' co-morbidities information to guide treatment options can cause some GPs not to adhere to recommendations with regard to antibiotic choice, dose, frequency or duration as in Straand *et al.* (1998), Kahan *et al.* (2005), Taur and Smith (2007), McIsaac *et al.* (2008), Llor *et al.* (2011), Vellinga *et al.* (2011), Denes *et al.* (2012) and Haasum *et al.* (2013). The presence of such details might justify some broad-spectrum antibiotic prescriptions, use of second-line antibiotics or altered durations. Fifth, the IMS-DA includes only antibiotics prescribed by GPs; it lacks the link with pharmacy dispensing data, therefore it cannot distinguish between antibiotics prescribed and antibiotics actually dispensed (Friis *et al.* 1989, Straand *et al.* 1998, Wrigley *et al.* 2002, Kahan *et al.* 2005, Petersen and Hayward 2007a, Taur and Smith 2007, McIsaac *et al.* 2008, Llor *et al.* 2011, Vellinga *et al.* 2011, Denes *et al.* 2012, Haasum *et al.* 2013). All five limitations might result in over- or underestimation of UTI prevalence, the patterns and trends of antibiotics and the magnitude of GPs' adherence to good practice points. One last limitation was related to the difficulty in comparing the results from the quantitative study with other published literature, either on a national or an international level, owing to there being limited published work on elderly patients in primary care, variations in the data sources, namely, laboratory data (McIsaac *et al.* 2008, Vellinga *et al.* 2011, Denes *et al.* 2012) versus computerised database (Wrigley *et al.* 2002, Kahan *et al.* 2005, Petersen and Hayward 2007a, Taur and Smith 2007, Haasum *et al.* 2013) versus survey (Ruben *et al.* 1995, Malmsten *et al.* 1997, Foxman *et al.* 2000, Molander *et al.* 2000), variations in the reporting units for prevalence such as percentage in (Molander *et al.* 2000, Galatti *et al.* 2006, Eriksson *et al.* 2010, Omoregie *et al.* 2010) or 100 person-years, per 1,000 per year or 10,000 person-years for incidence (Czaja *et al.* 2007, Laupland *et al.* 2007, Caljouw *et al.* 2011) and antibiotics prescribing between published work such as the use of DDD (Norris *et al.* 2011, Pan *et al.* 2011) or percentage (Wrigley *et al.* 2002, Kahan *et al.* 2005, Petersen and Hayward 2007a, Taur and Smith 2007, Haasum *et al.* 2013) and finally the recommendations in different countries, for instance, trimethoprim (Vellinga *et al.* 2011) versus fosfomycin (Llor *et al.* 2011).

### 6.4.2 Qualitative Study

Use of a phenomenographic approach, considered one of the strengths of this thesis, along with two different analytical techniques, made it possible to attain in-depth understanding of the phenomenon without adopting a predetermined hypothesis and allowing the findings to be derived inductively from the data obtained from the interviewed GPs' perspectives (Bruce 1994). The use of semi-structured interviews as the method of data collection for the qualitative research allowed understanding of the GPs' different standpoints through motivating them to speak for themselves using their own words and language to express their thoughts, views, concepts and perceptions about the phenomenon of antibiotics prescribing besides the factors that might affect their antibiotics prescribing from within their general practice context (Kvale 1996, Patton 2002). The research included over 1,160 minutes of digital recording (more than 600 pages of A4 transcript papers) representing the total length of semi-structured interviews with 17 GPs who were selected through non-probability purposive sampling that resulted in generating rich information and an in-depth representation of GPs' prescribing practice in the UK (Jupp 2006). The research was validated in relation to the quality of the collected data, the theoretical data saturation and the qualitative data analysis through review by external field experts other than the research team members.

#### 6.4.2.1 Trustworthiness of Qualitative Study

Trustworthiness was ensured by applying rigorous qualitative research criteria that were described in Chapter Three of this thesis. Transferability was achieved by providing clear and detailed description of how GPs were selected with different genders, years of experience and from different practice site locations, presenting GPs' demographics in the findings, with clear description of the research culture and context, data collection and the process of analysis as well as appropriate presentation of the findings and use of appropriate quotations. Although this research used a purposive sample to recruit GPs, its main aim was to explore and identify GPs' views and perceptions and to generate themes but not statements that are generalisable to other practitioners. In this research, credibility was ensured through the researcher's background and familiarity with the subject matter under investigation, adherence to the interview topic guide, proper presentation and rephrasing of open-ended interview questions, use of prompts and probes to encourage GPs to deepen and develop their thoughts and ideas, selection of GPs with different practice experience to increase the possibility of approaching the research aim from different perspectives, thick description of the phenomenon under investigation as well as interviewing GPs with different genders and ages, which maximised the variations and enriched the research. Since prescribing practice can be a sensitive topic to discuss with

GPs who might be aware of their deviation from what exists within the guidelines, their responses may have been biased to attempt to describe a more responsible and correct prescribing practice than actually exists. To attempt to minimise this effect, all GPs were reassured at the start of the interview that there were no right or wrong answers, that they were not going to be judged on their prescribing practice and that no consequences would result from anything revealed during the interviews. The GPs were relaxed and honest whenever they described issues related to their prescribing practice. Dependability was achieved through using the same introductory questions and additional questions with all interviewed GPs within a short period of time to ensure consistency, conducting a code–recode procedure on the data during the analysis phase of the study, that is, comparing the initial coding of the data with the recoding of the data after two weeks, and using external field experts, that is, educational experts, to check the data saturation point and research analysis in addition to supervisor as peer examination, to check the research plan and implementation. Confirmability was achieved by ensuring that what was said during the interviews was inextricably connected to how the GPs said it, by having two research team members work independently to check the quality and consistency of the data transcripts, data coding and interpretations then meeting regularly to discuss and resolve coding discrepancies and agree upon interpretation of the findings. In line with the recommendations from Lincoln and Guba (1985) and Ritchie *et al.* (2014), research external validity was strengthened by providing a thick description of all aspects of the research in this thesis, involving a detailed account of the methods and data analysis procedures and an in-depth presentation of the findings.

One of the strengths of the approach followed is that it was descriptive and interpretative, which enabled detection of new factors and views, as seen in Chapter Five. Owing to the fact that thematic analysis can result in de-contextualisation of the GPs’ words, careful consideration was undertaken during analysis of the GPs’ words in the broader context of the surrounding utterances to avoid any misinterpretation or presentation. This research represented the views about antibiotics prescribing for elderly patients of the 17 GPs from the UK, which may not be the same as the views of other GPs either in the UK or from other countries. Although data saturation was achieved, as evidenced by the emergence of the same views and themes throughout the interviews, caution was needed when generalising the findings. The GPs who agreed to take part in the qualitative research may have had a special interest in antibiotics, elderly patients or UTIs, making their responses skewed. To minimise this influence, the GPs were asked to provide a brief description of their qualifications, research interests and backgrounds. Only one GP showed an interest in UTIs and antibiotics as a result of previous work carried out during the GP's PhD study. The risk of bias may have been increased if the GPs had known the interviewer professionally or if the interviewer had a clinical background. To eliminate the risk of bias, the researcher recruited GPs who were totally unknown to him in addition to introducing himself as a clinical pharmacist and a PhD student.

## 6.5 Conclusions

The purpose of this thesis was to give a quantitative and qualitative account of how GPs prescribe antibiotics for elderly patients with UTIs in the UK. According to both the researcher's knowledge and the identified gaps in the previous research work, as highlighted in Chapter Two, this is one of the first studies in this field.

In conclusion, the research suggests that there is no available national guideline in the UK for the management of UTIs in elderly patients that provides specific recommendations on the best choice of antibiotic therapy according to the type of UTI based on evidence retrieved from studies performed particularly for elderly people. The newly introduced SAPG decision aid tool was built on summaries from previously published recommendations for adult patients with UTIs. The results from the research showed that UTIs were found to be more common in female elderly patients compared with males and the prevalence of UTIs seems to increase with advancing age in the elderly. Using DUR to audit antibiotics prescriptions showed that some UK GPs did not adhere to SAPG good practice points by prescribing broad-spectrum antibiotics, namely, cephalexin, co-amoxiclav and ciprofloxacin in 24.1% of all UTI antibiotics prescriptions. This should be avoided since these antibiotics can increase the susceptibility of elderly people to *Clostridium difficile* infection. Additionally, GPs prescribed antibiotics for durations other than those stated by the recommendations in 28% of trimethoprim prescriptions as well as 50.5% of nitrofurantoin prescriptions, or prescribed alternative drugs in particular for LUTIs. This practice could result in deterioration of elderly patients' conditions, exposing them to side effects and increase or development of bacterial resistance.

Qualitatively, five categories were identified from the phenomenographic analysis: perceptions, knowledge, decision, practice and approach. Of these, perception was found to be the most sophisticated view since it involves a wider context of this phenomenon.

Within these, there was substantial variation among the GPs' views. That said, it is normally accepted to see variations in perceptions within the same category, as each individual has a different life experience, as highlighted in Chapter Three. However, the presence of contrasting perceptions within the same category might explain why there is variation in antibiotics prescribing practice among GPs, which can be inappropriate too. The research has shown that some GPs tend to prescribe antibiotics for elderly patients more flexibly, more frequently and more quickly than for adult patients. Considering gender variation, some GPs were found to prescribe broad-spectrum antibiotics as well as altered choices and durations. Also, variation in GPs' knowledge and awareness of guidelines might indicate the presence of a problem in the dissemination process and may explain why GPs prescribe antibiotics inappropriately.

Until conducting this research, there was little evidence about the factors influencing antibiotics prescribing for UTIs in elderly patients (Lopez-Vazquez *et al.* 2012). This research identified a number of factors that belong to different contexts, mainly micro-level, that were identified as contributing to and influencing GPs' antibiotics prescribing practice. The research has shown that the factors cited by GPs were more related to adults compared with elderly patients, which could suggest a poor understanding of the elderly in terms of prescribing. Interestingly, some of these factors were novel and discussed for the first time from an antibiotics perspective.

This research has advanced the knowledge about GPs' antibiotics prescribing for UTIs in elderly patients. The findings highlighted the need for urgent, practical and efficient interventions to optimise and rationalise GPs' antibiotics prescribing for elderly patients. These should take the form of robust guidelines that should be easy, concise, representative to general practice contexts and developed by a panel. The guidelines should engage GPs through multifaceted intensive interventions aimed at improving prescribing practice for elderly patients and incorporate perceptions modification as part of their design, to reduce, or eliminate, if possible, any discrepancies in prescribing practice and to impact positively on GPs' inappropriate prescribing, non-adherence and, most importantly, reduce the threat of resistance in this context. Moreover, interventions should be targeted towards the seven external horizons that shape GPs' antibiotics prescribing practice perceptions. Healthcare bodies responsible for issuing guidelines, such as PHE and NICE, must issue specific guidelines or incorporate a separate section for the management of UTIs in elderly patients in primary care settings. Further research should investigate the influence of unexplored factors influencing GPs' antibiotics prescribing for elderly patients such as elderly autonomy, complacency, healthcare resources constraints and societal experience and expectations as well as the relationships between these factors and GPs' demographics, as these points have never been explored.

### 6.5.1 Original Contribution of this Research

The original contribution made by this research is threefold. First, it adds to the body of knowledge; second, it contributes to the research methodology; and third, it contributes to the strategies for improving antibiotics prescribing.

#### 6.5.1.1 Contribution to the Body of Knowledge

This research has advanced understanding and contributed to the body of knowledge about the prevalence of UTIs, GPs' patterns and trends of antibiotics prescribing, the quality of GPs' antibiotics prescribing for elderly patients with UTIs, and the understanding of GPs' perceptions and views, and has identified clinical and non-clinical factors that may influence GPs' antibiotics prescribing for elderly patients who visited GP surgeries in the UK.

#### 6.5.1.2 Contribution to the Research Methodology

This research has made an original contribution to the research methodology because it is the first to use phenomenographic approach with two methods of data analysis as a part of a mixed methods approach to discuss a sensitive topic with GPs. The interpretive and descriptive research paradigm made it possible to understand GPs' experiences of antibiotics prescribing practice in its original context from their own perspective by encouraging GPs to speak openly, to reflect and to share their experiences of prescribing.

#### 6.5.1.3 Theoretical Contribution

The original theoretical contribution is that this research has proposed a theoretical framework for developing antibiotics strategies incorporating findings from the mixed methods research. This approach was designed bearing in mind that changing GPs' behaviour is a lengthy, complex and difficult task. Therefore, the framework involves a combination of interventions that may provide tangible outcomes in the short term as well as in the long term (Figure 33).

## 6.6 Implications for Practice and Research

This research has contributed to the growing body of evidence suggesting that antibiotics are being widely prescribed by GPs in the UK, often with limited adherence to guidelines, recommendations or good practice points, which in turn raises concerns about the negative consequences of such practice such as financial, AMR, budgetary constraints, clinical outcomes, inefficiencies and distortion and behaviour of healthcare systems practice (Maragakis *et al.* 2008, Llor and Bjerrum 2014). The various results and findings from this research might have implications for future policy, practice and research. A number of suggested thoughts are given below.

Findings from this research highlighted the presence of variations in GPs' antibiotic prescribing practice including inappropriate prescribing by some GPs. Efforts to encourage GPs' rational prescribing of antibiotics for elderly patients in primary care should consider factors associated with patients, GPs, the healthcare system as well as society. Taking into consideration all these factors might help in designing practical interventions aimed at promoting appropriate antibiotics prescribing by GPs that may add to the current interventions implemented by the NHS such as antimicrobial stewardships. However, no single intervention was found to be influential by itself in curbing inappropriate prescribing; therefore a multifaceted approach targeting all these stakeholders would be more feasible for improving antibiotics prescribing for elderly patients taking into consideration the local contexts as shown in different qualitative research (Tonkin-Crine *et al.* 2011b, Duane *et al.* 2013) and a Cochrane systematic review (Arnold and Straus 2005).

As a part of this multifaceted intervention, there should be perceptions modification interventions to improve prescribing practice for elderly patients as they may influence GPs' attitudes and determine whether they will change their practice. Although changing human behaviour, habits and perceptions is recognised as being challenging, facilitating the process to modify behaviour is possible (Stålsby Lundborg and Tamhankar 2014). Such interventions might reduce, or eliminate, if possible, the contrasting views, thus overcoming any discrepancies in prescribing practice and impacting positively on GPs' inappropriate prescribing, non-adherence and making them responsible prescribers (Mustafa *et al.* 2014). Furthermore, narrowing the variation in GPs' concepts with regards to dimensions as was noted in GPs' views about AMR might improve prescribing practice. Furthermore, modification of GPs' perceptions may improve many aspects that may be associated with misperceptions such as patients' anticipation of antibiotics, patients' satisfaction, antibiotics cost, prescribing broad-spectrum antibiotics to improve patient condition or drugs being safe (McDonnell Norms Group 2008, Ashworth *et al.* 2016).

The interventions should also be targeted towards the seven external horizons that shape GPs' antibiotics prescribing practice through multifaceted educational and training programmes that start in the early stages of GPs' medical school education and future career. For example, increasing the number of credited hours for antibiotic pharmacology and elderly patients during undergraduate courses, exposing trainee GPs to more cases of elderly patients with infections during hospital training, providing CME-related material promoting rational antibiotics prescribing for elderly patients with confirmed infections, increasing antibiotics educational activities for GPs such as conferences, seminars and skills training programmes and motivating GPs to become more receptive in their practice. The influence of such interventions is supported by the findings from a RCT aimed at evaluating the effectiveness and costs of a multifaceted flexible educational programme consisting of various learning methods and topics for UK GPs to reduce antibiotics prescribing. The results from this study showed a successful reduction in antibiotics prescribing by 4.2% after implementing the educational programme (95% CI 0.6% to 7.7%) (Butler *et al.* 2012).

Another part of these multifaceted interventions should be introducing antibiotics prescribing guidelines specifically synthesised for the elderly population based on clinical trials, studies and evidence with representative samples of elderly patients (Singh and Bajorek 2014, Beckett *et al.* 2015). Increasing GPs' awareness, uptake and implementation of SAPG good practice points for UTIs should also be incorporated with perceptions change. GPs must be convinced with strong arguments why they should change their practice to become more evidence-based. GPs must be involved in the process of evidence synthesis because of their knowledge of the context of general practice, especially relating to guidelines targeting primary care practice. Moreover, guidelines must be more flexible and tailored to meet individual patient conditions and local practice settings, as in the case of elderly patients. Owing to GPs workload and time limits, guidelines must be accessible, useable, clear and concise with clear statements about evidence quality. Both the NHS and local CCGs should assure GPs that the developed guidelines are not synthesised for budgetary cuts over the quality of clinical services provided. Rewarding GPs who adhere to guidelines in the form of financial incentives or holidays might assist in increasing guideline uptake and facilitate GPs' behaviour change. Several qualitative and quantitative studies have discussed different strategies to change GPs' behaviour with regard to UTI guidelines and shared in many interventions (Lugtenberg *et al.* 2010, Willems *et al.* 2012, Demonchy *et al.* 2014) including those related to other infections, as highlighted by (Tonkin-Crine *et al.* 2013).

The NHS and CCGs should continue their successful role in promoting rational antibiotics prescribing through integrating their winning initiatives and tools in this framework. This can include updating and improving antimicrobial stewardship programmes, increasing the number of activities of local and national auditing and feedback and recruiting more prescribing advisors and medicine management teams, promoting cost-effectiveness philosophies over cost-saving practices and encouraging practices to become part of recently launched incentive schemes. Additionally, they should work on improving the logistics of care, for instance, reducing the time between requesting laboratory diagnostics and prescribing antibiotics or introducing rapid diagnostic tests. Although these interventions seem to be simple, the factors that influence antibiotics prescribing are engrained in all stakeholders including national governmental policy, which might make the process of transformation and change impossible in the short term.

This research has thrown up many thoughts and ideas in need of further investigation among elderly patients with UTIs. It is recommended that further quantitative research be undertaken in the following areas:

- Further research should be conducted to identify the factors responsible for the peak prevalence and frequent visits to GP surgeries in elderly patients aged 84–93.
- Another worthwhile idea would be to carry out a prospective, cohort population-based study to estimate the prevalence of UTIs, audit GPs' antibiotics prescribing and calculate the direct drug cost for elderly patients with UTIs using patients' clinical

presentation, laboratory information for MSU and culture and actual antibiotics dispensing data.

- It would be interesting to explore the national burden and long-term consequences of UTIs in the UK for this particular age group by linking existing medical records databases to the Hospital Episode Statistics (HSE) database. Medical records databases contain countless valuable pieces of information that can be utilised for further studies on elderly patients with UTIs within the context of GP surgeries.
- It is recommended that further research be undertaken to explore the impact of elderly patients' co-morbidities on GPs' antibiotics prescribing for UTIs including antibiotic choice, dose and duration of therapy. Drug utilisation studies might be a valuable research method for providing insight into GPs' antibiotics prescribing as they can be used to improve the quality of prescribing.
- Considerably more work needs to be done to evaluate the impact of introducing a national drug utilisation programme or a computerised system for improving the quality of GPs' antibiotics prescribing against predetermined audit criteria. This could be very useful in providing GPs with feedback about their prescribing practice and minimising variations in prescribing, both locally and nationally.
- It would be very interesting to carry out future research to design, implement and evaluate the effectiveness of various multifaceted interventions for improving antibiotics prescribing for elderly patients in primary care. However, as in all implementation research, the context is of great importance, whereas local validations of interventions will always be required.

Qualitative research is becoming routine in healthcare studies, assuming the main role of exploring complex topics and defining new approaches to the targeted field (Jack 2006). Qualitative research should address antibiotics prescribing for elderly patients with UTIs in the following areas:

- As this qualitative research included only 17 GPs perhaps the findings should be tested and refined over a larger number of GPs from different countries, perhaps with other types of interview question and using different qualitative methods and different analytical approaches to gain a deeper understanding of GPs' prescribing habits and behaviour.
- Although this thesis explored the perceptions of GPs regarding antibiotics prescribing for elderly patients, more complex research needs to involve GPs, patients, families,

carers and healthcare decision-makers to fully understand the perceptions of antibiotics prescribing, in interaction within a complex, social context. Socio-cultural theories may offer a useful framework for future research by providing a lens that can accommodate the wide range of interacting factors influencing GPs' prescribing habits and behaviour.

- Another area worth exploring is the impact of specific factors on antibiotics prescribing by GPs by dedicating a complete research study to each factor. The factors may include the impact of elderly patients' autonomy and expectations on GPs' antibiotics prescribing; the impact of scheme incentives on GPs' antibiotics prescribing; the influence of secondary care doctors on GPs' antibiotics prescribing; and habits of adoption and the influence of ageing on GPs' antibiotics prescribing.
- Exploring GPs' views and perceptions of having specifically developed guidelines for elderly patients is another good research theme.
- It would be interesting to explore the impact of different multifaceted interventions on GPs' antibiotics prescribing for elderly patients.
- Considerably more work needs to be done by using other methodological approaches for future research such as a multilevel analysis of patients' and GPs' factors, recognising the lack of some findings from GPs such as the importance of finishing a course of antibiotic and some of the limitations for using a London based sample for the qualitative research.
- Finally, research could explore the impact of GPs' demographics and personal characteristics on their perceptions and prescribing practice for elderly patients in the form of phenomenographic and ethnographic study.

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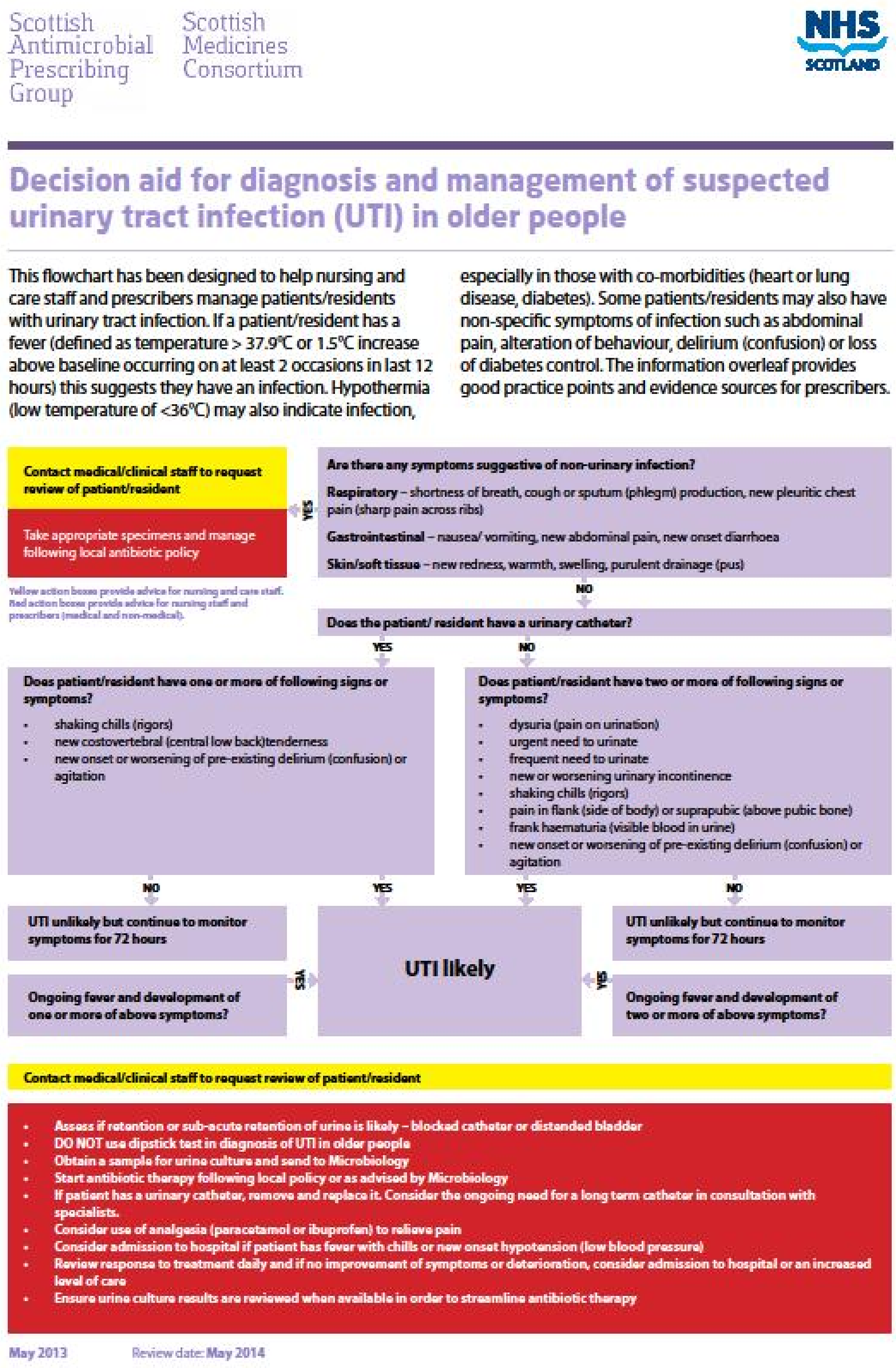
# Appendix

## Appendix 1. Oral and parenteral antibiotic regimens for the treatment of UTIs (Nicolle 2009a)

| | |
|---|---|
| | **Oral** |
| **Antibiotic** | **Dose*** |
| **First-line** | |
| Nitrofurantoin | 50–100 mg four times a day |
| TMP-SMX | 160/800 mg, twice daily |
| TMP | 100 mg twice daily |
| Amoxicillin | 500 mg three times daily |
| **Others** | |
| Co-amoxiclav | 500 mg three times daily or 875 mg twice daily |
| Norfloxacin | 400 mg twice daily |
| Ciprofloxacin | 250–500 mg twice daily |
| Ofloxacin | 200–400 mg twice daily |
| Levofloxacin | 500 mg once a day |
| Cephalexin | 500 mg four times a day |
| Cefaclor | 500 mg |
| Cefadroxil | 1 g once a day or twice daily |
| Cefixime | 400 mg once a day |
| Cefuroxime axetil | 250 mg twice daily |
| Cefpodoxime proxetil | 100–400 mg twice daily |
| | **Parenteral** |
| **Preferred** | |
| Gentamicin | 1.5–1mg/kg q8h or 4–5 mg/kg q24h |
| Tobramycin | 1.5–1mg/kg q8h or 4–5 mg/kg q24h |
| Ampicillin | 1g q4–6h |
| Cefazolin | 1–2 g q8h |
| **Others** | |
| TMP-SMX | 16- 800/mg q12h |
| Amikacin | 5mg/kg q8h or 15 mg/kg q24h |
| Piperacillin | 3g q4h |
| Piperacillin-tazobactam | 4g-500 mg q8h |
| Cefotaxime | 2–1g q8h |
| Ceftriaxone | 2–1g q24h |
| Cefepime | 2g q12h |
| Ceftazidime | 2–0.5g q8h |
| Aztreonam | 2–1g q6h |
| Imipenem/cilastatin | 500mg q6h |
| Vancomycin | 500mg q6h or l g q12h |
| Ciprofloxacin | 400–200mg q12h |
| Levofloxacin | 500 mg daily |

* Assuming normal renal function; Q: every

# Appendix 2 Decision aid for diagnosis and management of suspected urinary tract infection (UTI) in older people (SAPG 2013)



Scottish Antimicrobial Prescribing Group

Scottish Medicines Consortium

NHS SCOTLAND

## Decision aid for diagnosis and management of suspected urinary tract infection (UTI) in older people

This flowchart has been designed to help nursing and care staff and prescribers manage patients/residents with urinary tract infection. If a patient/resident has a fever (defined as temperature > 37.9°C or 1.5°C increase above baseline occurring on at least 2 occasions in last 12 hours) this suggests they have an infection. Hypothermia (low temperature of <36°C) may also indicate infection, especially in those with co-morbidities (heart or lung disease, diabetes). Some patients/residents may also have non-specific symptoms of infection such as abdominal pain, alteration of behaviour, delirium (confusion) or loss of diabetes control. The information overleaf provides good practice points and evidence sources for prescribers.

**Are there any symptoms suggestive of non-urinary infection?**

**Respiratory** – shortness of breath, cough or sputum (phlegm) production, new pleuritic chest pain (sharp pain across ribs)

**Gastrointestinal** – nausea/ vomiting, new abdominal pain, new onset diarrhoea

**Skin/soft tissue** – new redness, warmth, swelling, purulent drainage (pus)

YES

**Contact medical/clinical staff to request review of patient/resident**

Take appropriate specimens and manage following local antibiotic policy

Yellow action boxes provide advice for nursing and care staff. Red action boxes provide advice for nursing staff and prescribers (medical and non-medical).

NO

**Does the patient/ resident have a urinary catheter?**

YES

**Does patient/resident have one or more of following signs or symptoms?**

- shaking chills (rigors)
- new costovertebral (central low back)tenderness
- new onset or worsening of pre-existing delirium (confusion) or agitation

NO

**Does patient/resident have two or more of following signs or symptoms?**

- dysuria (pain on urination)
- urgent need to urinate
- frequent need to urinate
- new or worsening urinary incontinence
- shaking chills (rigors)
- pain in flank (side of body) or suprapubic (above pubic bone)
- frank haematuria (visible blood in urine)
- new onset or worsening of pre-existing delirium (confusion) or agitation

NO

**UTI unlikely but continue to monitor symptoms for 72 hours**

**Ongoing fever and development of one or more of above symptoms?**

YES

**UTI likely**

YES

**UTI unlikely but continue to monitor symptoms for 72 hours**

**Ongoing fever and development of two or more of above symptoms?**

**Contact medical/clinical staff to request review of patient/resident**

- **Assess if retention or sub-acute retention of urine is likely – blocked catheter or distended bladder**
- **DO NOT use dipstick test in diagnosis of UTI in older people**
- **Obtain a sample for urine culture and send to Microbiology**
- **Start antibiotic therapy following local policy or as advised by Microbiology**
- **If patient has a urinary catheter, remove and replace it. Consider the ongoing need for a long term catheter in consultation with specialists.**
- **Consider use of analgesia (paracetamol or ibuprofen) to relieve pain**
- **Consider admission to hospital if patient has fever with chills or new onset hypotension (low blood pressure)**
- **Review response to treatment daily and if no improvement of symptoms or deterioration, consider admission to hospital or an increased level of care**
- **Ensure urine culture results are reviewed when available in order to streamline antibiotic therapy**

May 2013 Review date: May 2014

## Good practice points

### Urine culture

- Older people often have asymptomatic bacteriuria (no symptoms but bacteria in urine) which does not indicate infection.
- Do not send catheter specimens of urine (CSU) unless patient has signs and symptoms of infection as CSU samples will almost always have bacteriuria (bacteria in urine).
- Review urine culture results to check organism is sensitive to antibiotic prescribed and change to an alternative antibiotic if necessary.
- Interpretation of the urine culture results – high epithelial cell count or heavy mixed growth may indicate contamination. Ensure correct sampling process is followed and take repeat urine sample if clinically indicated.
- Be alert to UTI due to resistant organisms such as Extended Spectrum Beta-Lactamase *E. coli*. Microbiology will provide advice on treatment options. In patients with a previous ESBL UTI discuss with Microbiology the potential treatment options should the patient become symptomatic again.
- Do not send urine samples for post-antibiotic checks or clearance of infection.

### Antibiotic therapy

- Older people are vulnerable to infection, particularly *Clostridium difficile* infection, therefore use of broad spectrum antibiotics such as ciprofloxacin, co-amoxiclav and cephalosporins should be avoided if possible.
- First choice antibiotics for uncomplicated lower UTI in non-catheterised patients are trimethoprim 200mg twice daily or nitrofurantoin 50mg four times daily (or nitrofurantoin MR 100mg twice daily). Recommended course duration is three days for women and seven days for men.
- Avoid nitrofurantoin in patients with renal impairment (BNF suggests avoid if eGFR < 60 ml/min/1.73m3)
- In men, if there is clinical suspicion of acute prostatitis (suggested by fever and pain at the base of the penis, around the anus, just above the pubic bone and/or in the lower back), a 28 day course of ciprofloxacin or ofloxacin is recommended. Trimethoprim may be used if the organism is sensitive.
- In catheterised patients with symptoms of UTI, a seven day course of antibiotics, following local antibiotic guidelines is recommended in both men and women. The catheter should be removed then replaced if necessary.
- Second choice antibiotics should always be guided by urine culture and history of antibiotic use.

### Prophylaxis of UTI

- The evidence base supporting antibiotic use for prophylaxis of UTI is ***not strong***; all studies were conducted pre-2000 and none evaluated patients beyond one year.
- Female patients who do not have a catheter and have more than three UTIs within a 12 month period ***may*** be considered for a trial of nightly antibiotic prophylaxis with trimethoprim or nitrofurantoin. The risk of adverse effects versus the potential benefit needs to be considered carefully.
- Long term antibiotics prescribed for UTI prophylaxis do promote resistance and there is no evidence to support their use beyond 6-12 months. Therefore ongoing clinical need should be reviewed after 6 months.
- Cranberry products may be considered as an alternative but evidence of their efficacy is lacking.
- In post-menopausal women consider the possibility of recurrent symptoms being associated with vaginal atrophy.

References


1. Lohfeld L, Loeb M, Brazil K, Evidence-based clinical pathways to manage urinary tract infections in long-term care facilities: a qualitative case study describing administrator and nursing staff views. J Am Med Dir Assoc 2007; 8: 477–484
2. Loeb M, Brazil K, Lohfeld L, McGeer A, Simor A, Stevenson K, et al. Effect of a multifaceted intervention on number of antimicrobial prescriptions for suspected urinary tract infections in residents of nursing homes: cluster randomised controlled trial. BMJ 2005;331(7518):669.
3. Scottish Intercollegiate Guideline Network, Guideline 88 Management of Bacterial Urinary Tract Infection http://www.sign.ac.uk/pdf/sign88.pdf
4. Health Protection Agency, Diagnosis of UTI – Quick Reference Guide for Primary Care http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1194947404720
5. Health Protection Agency, Management of Infection Guidance for Primary Care, http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1279888711402

# Appendix 3. Key terms and search strategy used for literature search

## Appendix 3.1: Search terms and strategy for UTI epidemiology in elderly patients

1/11/2016 Ovid: Search Results

Database(s): **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present

Search Strategy:

| # | Searches | Results | Annotations |
|---|---|---|---|
| 1 | "Urinary Tract Infections/ or urinary tract infection*.mp. | 48878 | |
| 2 | "Cystitis/ or cystitis.mp. | 12365 | |
| 3 | "Pyelonephritis/ or pyelonephritis.mp. | 18082 | |
| 4 | UTI*.mp. | 625325 | |
| 5 | 1 or 2 or 3 or 4 | 689945 | |
| 6 | geriatric*.mp. | 85278 | |
| 7 | "Aged/ or "Aging/ or ""Aged, 80 and over"/ or ageing.mp. | 165605 | |
| 8 | elder*.mp. | 213116 | |
| 9 | 6 or 7 or 8 | 400817 | |
| 10 | primary care.mp. or "Primary Health Care/ | 101346 | |
| 11 | primary medical care.mp. or "Family Practice/ | 41001 | |
| 12 | Ambulatory Care.mp. or "Ambulatory Care/ | 58260 | |
| 13 | Community Health Centers/ or Community Health Cent*.mp. | 8272 | |
| 14 | 10 or 11 or 12 or 13 | 195536 | |
| 15 | Family Practice/ or Physicians, Family/ or General Practice/ or General Practitioner*.mp. | 106524 | |
| 16 | epidemiology.mp. or Epidemiology/ | 178772 | |
| 17 | incidence.mp. or "Incidence/ | 679222 | |
| 18 | "Prevalence/ or prevalence.mp. | 530400 | |
| 19 | 16 or 17 or 18 | 1269551 | |
| 20 | 5 and 9 and 14 and 15 and 19 | 46 | |

https://ovidsp.uk.ovid.com/sp-3.20.0b/ovidweb.cgi

## Appendix 3.2: Search terms and strategy for GPs antibiotics drug utilisation for UTI in elderly patients

1/11/2016 Ovid: Search Results

Database(s): **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present

Search Strategy:

| # | Searches | Results | Annotations |
|---|---|---|---|
| 1 | *Urinary Tract Infections/ or urinary tract infection*.mp. | 48878 | |
| 2 | *Cystitis/ or cystitis.mp. | 12365 | |
| 3 | *Pyelonephritis/ or pyelonephritis.mp. | 18082 | |
| 4 | UTI*.mp. | 625325 | |
| 5 | 1 or 2 or 3 or 4 | 689945 | |
| 6 | geriatric*.mp. | 85278 | |
| 7 | *Aged/ or *Aging/ or *"Aged, 80 and over"/ or ageing.mp. | 165605 | |
| 8 | elder*.mp. | 213116 | |
| 9 | 6 or 7 or 8 | 400817 | |
| 10 | primary care.mp. or *Primary Health Care/ | 101346 | |
| 11 | primary medical care.mp. or *Family Practice/ | 41001 | |
| 12 | Ambulatory Care.mp. or *Ambulatory Care/ | 58260 | |
| 13 | Community Health Centers/ or Community Health Cent*.mp. | 8272 | |
| 14 | 10 or 11 or 12 or 13 | 195536 | |
| 15 | Family Practice/ or Physicians, Family/ or General Practice/ or General Practitioner*.mp. | 106524 | |
| 16 | antibiotic*.mp. or *Anti-Bacterial Agents/ | 378893 | |
| 17 | antimicrobial*.mp. | 116617 | |
| 18 | *Anti-Infective Agents/ or antiinfective*.mp. | 32377 | |
| 19 | 16 or 17 or 18 | 462325 | |
| 20 | Drug Utilization/ or Practice Patterns, Physicians'/ or drug utilization*.mp. | 65686 | |
| 21 | drug utilisation.mp. or "Drug Utilization Review"/ | 3578 | |
| 22 | drug utilisation.mp. or *"Drug Utilization Review"/ | 2176 | |
| 23 | drug consumption*.mp. | 2198 | |
| 24 | drug prescribing.mp. or *Drug Prescriptions/ | 14466 | |
| 25 | 20 or 21 or 22 or 23 or 24 | 78047 | |
| 26 | 5 and 9 and 14 and 15 and 19 and 25 | 5 | |

https://ovidsp.uk.ovid.com/sp-3.20.0b/ovidweb.cgi

## Appendix 3.3: Search terms and strategy for GPs adherence to antibiotics prescribing guidelines for treating UTIs in elderly patients



Database(s): **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present

Search Strategy:

| # | Searches | Results | Annotations |
|---|---|---|---|
| 1 | *Urinary Tract Infections/ or urinary tract infection*.mp. | 48878 | |
| 2 | *Cystitis/ or cystitis.mp. | 12365 | |
| 3 | *Pyelonephritis/ or pyelonephritis.mp. | 18082 | |
| 4 | UTI*.mp. | 625325 | |
| 5 | 1 or 2 or 3 or 4 | 689945 | |
| 6 | geriatric*.mp. | 85278 | |
| 7 | *Aged/ or *Aging/ or *"Aged, 80 and over"/ or ageing.mp. | 165605 | |
| 8 | elder*.mp. | 213116 | |
| 9 | 6 or 7 or 8 | 400817 | |
| 10 | primary care.mp. or *Primary Health Care/ | 101346 | |
| 11 | primary medical care.mp. or *Family Practice/ | 41001 | |
| 12 | Ambulatory Care.mp. or *Ambulatory Care/ | 58260 | |
| 13 | Community Health Centers/ or Community Health Cent*.mp. | 8272 | |
| 14 | 10 or 11 or 12 or 13 | 195536 | |
| 15 | Family Practice/ or Physicians, Family/ or General Practice/ or General Practitioner*.mp. | 106524 | |
| 16 | prescribing.mp. | 32790 | |
| 17 | *Prescription Drugs/ or Prescription*.mp. | 85712 | |
| 18 | 16 or 17 | 104499 | |
| 19 | antibiotic*.mp. or *Anti-Bacterial Agents/ | 378893 | |
| 20 | antimicrobial*.mp. | 116617 | |
| 21 | *Anti-Infective Agents/ or antiinfective*.mp. | 32377 | |
| 22 | 19 or 20 or 21 | 462325 | |
| 23 | *Guideline Adherence/ or adherence.mp. | 109718 | |
| 24 | 5 and 9 and 14 and 15 and 18 and 22 and 23 | 1 | |

**Appendix 3.4: Search terms and strategy for variations in GPs' antibiotics prescribing perceptions and views for UTIs in elderly patients**

1/11/2016 Ovid: Search Results

Database(s): **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present

Search Strategy:

| # | Searches | Results | Annotations |
|---|---|---|---|
| 1 | *Urinary Tract Infections/ or urinary tract infection*.mp. | 48878 | |
| 2 | *Cystitis/ or cystitis.mp. | 12365 | |
| 3 | *Pyelonephritis/ or pyelonephritis.mp. | 18082 | |
| 4 | UTI*.mp. | 625325 | |
| 5 | 1 or 2 or 3 or 4 | 689945 | |
| 6 | geriatric*.mp. | 85278 | |
| 7 | *Aged/ or *Aging/ or *"Aged, 80 and over"/ or ageing.mp. | 165605 | |
| 8 | elder*.mp. | 213116 | |
| 9 | 6 or 7 or 8 | 400817 | |
| 10 | primary care.mp. or *Primary Health Care/ | 101346 | |
| 11 | primary medical care.mp. or *Family Practice/ | 41001 | |
| 12 | Ambulatory Care.mp. or *Ambulatory Care/ | 58260 | |
| 13 | Community Health Centers/ or Community Health Cent*.mp. | 8272 | |
| 14 | 10 or 11 or 12 or 13 | 195536 | |
| 15 | Family Practice/ or Physicians, Family/ or General Practice/ or General Practitioner*.mp. | 106524 | |
| 16 | perception*.mp. or *Perception/ | 339104 | |
| 17 | view*.mp. | 376776 | |
| 18 | *Attitude/ or Attitude*.mp. | 346045 | |
| 19 | *Health Behavior/ or *Health Knowledge, Attitudes, Practice/ or Behaviour*.mp. | 273201 | |
| 20 | *Behavior/ or *Health Behavior/ or Behavior*.mp. | 1100306 | |
| 21 | 16 or 17 or 18 or 19 or 20 | 2052621 | |
| 22 | prescribing.mp. | 32790 | |
| 23 | *Prescription Drugs/ or Prescription*.mp. | 85712 | |
| 24 | 22 or 23 | 104499 | |
| 25 | 5 and 9 and 14 and 15 and 21 and 24 | 15 | |

https://ovidsp.uk.ovid.com/sp-3.20.0b/ovidweb.cgi

## Appendix 3.5: Search terms and strategy for Factors influencing GPs antibiotics prescribing for UTIs in elderly patients

1/11/2016 Ovid: Search Form

Ovid

Wolters Kluwer

My Account | Support & Training | Help | Logged in as HUSSAIN ALOMAR at KCL | Logoff

Search | Journals | Books | My Workspace | Visible Body | Multimedia

▾ Search History (33) View Saved

| # ▲ | Searches | Results | Type | Actions |
|---|---|---|---|---|
| 1 | *Urinary Tract Infections/ or urinary tract infection*.mp. | 48878 | Advanced | Display Results \| More ▾ |
| 2 | *Cystitis/ or cystitis.mp. | 12365 | Advanced | Display Results \| More ▾ |
| 3 | *Pyelonephritis/ or pyelonephritis.mp. | 18082 | Advanced | Display Results \| More ▾ |
| 4 | UTI*.mp. | 625325 | Advanced | Display Results \| More ▾ |
| 5 | 1 or 2 or 3 or 4 | 689945 | Advanced | Display Results \| More ▾ |
| 6 | geriatric*.mp. | 85278 | Advanced | Display Results \| More ▾ |
| 7 | *Aged/ or *Aging/ or *"Aged, 80 and over"/ or ageing.mp. | 165605 | Advanced | Display Results \| More ▾ |
| 8 | elder*.mp. | 213116 | Advanced | Display Results \| More ▾ |
| 9 | 6 or 7 or 8 | 400817 | Advanced | Display Results \| More ▾ |
| 10 | primary care.mp. or *Primary Health Care/ | 101346 | Advanced | Display Results \| More ▾ |
| 11 | primary medical care.mp. or *Family Practice/ | 41001 | Advanced | Display Results \| More ▾ |
| 12 | Ambulatory Care.mp. or *Ambulatory Care/ | 58260 | Advanced | Display Results \| More ▾ |
| 13 | Community Health Centers/ or Community Health Cent*.mp. | 8272 | Advanced | Display Results \| More ▾ |
| 14 | 10 or 11 or 12 or 13 | 195536 | Advanced | Display Results \| More ▾ |
| 15 | Family Practice/ or Physicians, Family/ or General Practice/ or General Practitioner*.mp. | 108524 | Advanced | Display Results \| More ▾ |
| 16 | perception*.mp. or *Perception/ | 339104 | Advanced | Display Results \| More ▾ |
| 17 | view*.mp. | 376776 | Advanced | Display Results \| More ▾ |
| 18 | *Attitude/ or Attitude*.mp. | 348045 | Advanced | Display Results \| More ▾ |
| 19 | *Health Behavior/ or *Health Knowledge, Attitudes, Practice/ or Behaviour*.mp. | 273201 | Advanced | Display Results \| More ▾ |
| 20 | *Behavior/ or *Health Behavior/ or Behavior*.mp. | 1100306 | Advanced | Display Results \| More ▾ |
| 21 | 16 or 17 or 18 or 19 or 20 | 2052621 | Advanced | Display Results \| More ▾ |
| 22 | prescribing.mp. | 32790 | Advanced | Display Results \| More ▾ |
| 23 | *Prescription Drugs/ or Prescription*.mp. | 85712 | Advanced | Display Results \| More ▾ |
| 24 | 22 or 23 | 104499 | Advanced | Display Results \| More ▾ |
| 25 | factor*.mp. | 4585947 | Advanced | Display Results \| More ▾ |
| 26 | driver*.mp. | 36480 | Advanced | Display Results \| More ▾ |
| 27 | influenc*.mp. | 1147503 | Advanced | Display Results \| More ▾ |
| 28 | 25 or 26 or 27 | 5332832 | Advanced | Display Results \| More ▾ |
| 29 | antibiotic*.mp. or *Anti-Bacterial Agents/ | 378893 | Advanced | Display Results \| More ▾ |
| 30 | antimicrobial*.mp. | 116617 | Advanced | Display Results \| More ▾ |
| 31 | *Anti-Infective Agents/ or antiinfective*.mp. | 32377 | Advanced | Display Results \| More ▾ |
| 32 | 29 or 30 or 31 | 462325 | Advanced | Display Results \| More ▾ |
| 33 | 5 and 9 and 14 and 15 and 21 and 24 and 28 and 32 | 0 | Advanced | Remove \| More ▾ |

Save | Remove | Combine with: AND | OR

Save All | Create RSS | View Saved

Basic Search | **Advanced Search** | Find Citation | Search Tools | Search Fields | Multi-Field Search

1 Resource selected | Hide | Change

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present

Enter keyword or phrase (* or $ for truncation) ◉ Keyword ○ Author ○ Title ○ Journal

Search

▸ Limits (expand) ☐ Include Multimedia ☑ Map Term to Subject Heading

To search Open Access content on Ovid, go to Basic Search.

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## Appendix 4. Comparison of data supplied by the three databases in the UK (Ogdie *et al.* 2012, UCL 2013, Matcho *et al.* 2014)

| Database | Data | Example of contents |
|---|---|---|
| CPRD | **Patient** | Patient identifier, month and year of birth, registration status, death date, transfer out date |
| | **Practice** | Practice identifier, geographical region, date practice became 'Up to standard', last data collection date |
| | **Staff** | Staff identifier, gender, role |
| | **Consultation** | Date of clinical event, date of data entry, type of consultation, staff identifier and duration of consultation |
| | **Clinical** | Date of clinical event, date of data entry, the CPRD medical code for the chosen Read code, additional details identifier, entity type |
| | **ACD** | Type of information held, called an 'entity', specific clinical details relating to that entity |
| | **Referral** | The CPRD medical code for the chosen Read code, method of referral, referral specialty, urgency of referral |
| | **Immunisation** | Reason for immunisation, type, stage, status and the compound used |
| | **Test** | Type of test, result, normal range of result, unit of measure |
| | **Links to external data** | CPRD data linked with HES |
| | **Therapy** | The CPRD product code for the medication, BNF code, quantity of product, dose, pack size, number of days prescribed |
| THIN | **Demographics** | Date patient registered at practice, date patient left practice, patient registration status, year of birth, gender, patients residing at the same addre or members of the same family linked if at the same practice using a household identifier number. Data not included (name, exact address or postcode, exact date of birth (year can be given), NHS number |
| | **Diagnoses** | Medical diagnoses for all conditions and symptoms, date of diagnosis, and location (e.g., GP's office, hospital, consultant) of the event and adding free text (optional); referrals to hospitals and specialists.<br>Secondary care information and other related information received by the practice, including (details on hospital, admissions, discharge medication and diagnosis, outpatient consultation diagnosis, investigation and treatment outcomes)<br>THIN data linked with HES. |
| | **Prescribing** | All prescriptions along with the date issued, formulation, strength, quantity, and dosing instructions, indication for treatment for all new prescriptions (inferred from cross reference to medical events on the same date), and events leading to withdrawal of a drug or treatment. |
| | **AHD** | Vaccinations and prescription contraceptives; smoking, height, weight, immunizations, pregnancy, birth, death, and laboratory results. |
| | **Free Text Comments** | Free text fields that can contain confidential or identifying information that is pseudonymised by THIN. |
| | **Socioeconomic/PVI** | Postcode linked area based socio-economic, ethnicity and environmental indices |
| | **Links to external data** | THIN data linked with HES |
| IMS-DA | **Practice** | Regional health authority, town size, patients per practice in the current quarter, patients per practice in the last quarter, drug-dispensing f number of GPs |
| | **Doctor** | Active status, age, sex, date of birth, doctor registration year, trainer status |
| | **Patient** | Age, sex, height, weight and BMI, marital status, registration status, regional health authority |
| | **Consultation day** | Date of visit |
| | **Clinical records** | Read codes and text, ICD-10 codes and text, referral records, sick notes, tests, further diagnosis and symptoms, history of or family history |
| | **Therapy records** | Medication, manufacturer, ATC, product (brand and generic name), pack form, therapy text (Read code), price, pack size, form and strength, recommended dosages, therapy stop |

ACD: Additional Clinical Details; AHD: Additional Health Data; PVI: Postcode variable indicators; BNF: British National Formulary; HSE: Hospital Episode Statistics; BMI: Body Mass Index; ICD-10: International Statistical Classification of Diseases and Related Health Problems

# Appendix 5. IMS-DA Read codes dictionary for UTIs Study

| Code | Description | Code | Description |
|---|---|---|---|
| Kyu6. | [X]Disease/male genital organs | 14D4. | H/O: recurrent cystitis |
| Kyu50 | [X]Other chronic cystitis | 14D7. | H/O: recurrent UTI |
| Kyu51 | [X]Other cystitis | 8D74. | Indwelling urethral catheter |
| K150. | Acute cystitis | K10z. | Infection of kidney NOS |
| 14D2. | H/O: kidney infection | K10.. | Infections of kidney |
| 68D2. | Asympt. bacteriuria screen | K1021 | Perinephric abscess |
| K1900 | Bacteriuria,site not specified | K1902 | Post-operative UTI |
| 4JJ4. | Catheter urine -> culture. | K10y4 | Pyelitis + disease EC |
| K1001 | Chr.pyelonephr.+medullary necr | K10y1 | Pyelitis unspecified |
| K1000 | Chr.pyelonephr.-no medull.necr | K10y3 | Pyelonephritis + disease EC |
| K1005 | Chron obstructv pyelonephritis | K10yz | Pyelonephritis unspecif.NOS |
| K152y | Chronic cystitis unspecified | K10y0 | Pyelonephritis unspecified |
| A9831 | Chronic gonococcal cystitis | K10y. | Pyelonephritis/pyonephr.unspec |
| K151z | Chronic interstit.cystitis NOS | K103. | Pyeloureteritis cystica |
| K151. | Chronic interstitial cystitis | K10y2 | Pyonephrosis unspecified |
| K1002 | Chronic pyelitis | K1901 | Pyuria, site not specified |
| K100. | Chronic pyelonephritis | 1AG | Recur urinary tract infections |
| K100z | Chronic pyelonephritis NOS | K155. | Recurrent cystitis |
| K1003 | Chronic pyonephrosis | K1903 | Recurrent urinary tract infecn |
| K1904 | Chronic urinary tract infectn | K1020 | Renal abscess |
| K15.. | Cystitis | K102. | Renal and perinephric abscess |
| K1540 | Cystitis + actinomycosis | K102z | Renal/perinephric abscess NOS |
| K1541 | Cystitis + amoebiasis | 1J4.. | Suspected UTI |
| K1542 | Cystitis + bilharziasis | K190z | Urinary tract infect.unsp.NOS |
| K1544 | Cystitis + diphtheria | K190. | Urinary tract infect.unsp.site |
| K1543 | Cystitis + echinococcus infest | K1905 | Urinary tract infection |
| K1545 | Cystitis + gonorrhoea | K1012 | Acute pyelitis |
| K1546 | Cystitis + moniliasis | K1011 | Acute pyelitis |
| K1547 | Cystitis + trichomoniasis | K1010 | Acute pyelitis |
| K1548 | Cystitis + tuberculosis | K101. | Acute pyelonephritis |
| K15y0 | Cystitis cystica | K101z | Acute pyelonephritis NOS |
| K154. | Cystitis in diseases EC | K1530 | Acute trigonitis |
| K154z | Cystitis in diseases EC NOS | K1004 | Nonobstr rflx/ass chrn pyelnph |
| K15z. | Cystitis NOS | K152. | Other chronic cystitis |
| A32y3 | Diphtheritic cystitis | K152z | Other chronic cystitis NOS |
| Q001. | Fetus+mat.renal/urinary diseas | K15yz | Other cystitis NOS |

## Appendix 6. Patients extracted information from IMS-DA and used for DUR study

1. Practice identifier
2. Patient identifier
3. Date of prescription
4. Read code level 4 or 5
5. ICD-10 code level 4
6. ATC code level 4
7. Product name
8. Name of product form
9. Strength
10. Unit of strength
11. Volume
12. Unit of volume
13. Package size
14. Drug substance
15. Prescribed quantity
16. Unit of prescribed quantity
17. Measurement unit of prescribed quantity
18. Daily dosage
19. Unit of daily dosage
20. Measurement unit of daily dosage
21. Duration (days)
22. Read code description
23. Sex
24. Date of birth (year)
25. Birth year
26. Start of follow up period
27. End of follow up period
28. Year of prescription
29. Age at event

## Appendix 7. E*ph*MRA AT main therapeutics group for antibacterial agents used in IMS-DA

| ATC Code | Drug Substance Name |
|---|---|
| **G4A** | **URINARY ANTI-INFECTIVES AND ANTISEPTICS** |
| G4A1 | Urinary antibacterials |
| G4A2 | Urinary non-halogenated quinolones |
| G4A3 | Out of use; can be reused from 2010 |
| G4A9 | Other urinary antiseptics |
| G4B | Out of use; can be reused from 201 |
| **J** | **GENERAL ANTI-INFECTIVES SYSTEMIC** |
| J1 | SYSTEMIC ANTIBACTERIALS |
| J1A | TETRACYCLINES AND COMBINATIONS |
| J1B | CHLORAMPHENICOL AND COMBINATIONS |
| J1C | BROAD SPECTRUM PENICILLINS |
| J1C1 | Oral broad spectrum penicillins |
| J1C2 | Injectable broad spectrum penicillins |
| J1D | CEPHALOSPORINS |
| J1D1 | Oral cephalosporins |
| J1D2 | Injectable cephalosporins |
| J1E | TRIMETHOPRIM AND SIMILAR FORMULATIONS |
| J1F | MACROLIDES AND SIMILAR TYPES |
| J1G | FLUOROQUINOLONES |
| J1G1 | Oral fluoroquinolones |
| J1G2 | Injectable fluoroquinolones |
| J1H | MEDIUM AND NARROW SPECTRUM PENICILLINS |
| J1H1 | Plain medium and narrow spectrum penicillins |
| J1H2 | Penicillin/streptomycin combinations |
| J1J | Out of use; can be reused. |
| J1K | AMINOGLYCOSIDES |
| J1L | CARBENICILLIN AND SIMILAR TYPES |
| J1M | RIFAMPICIN/RIFAMYCIN |
| J1N | Out of use; can be re-used from 1997 |
| J1P | OTHER BETA-LACTAM ANTIBACTERIALS, EXCLUDING PENICILLINS, CEPHALOSPORINS |
| J1P1 | Monobactams |
| J1P2 | Penems and carbapenems |
| J1P3 | Carbacephems |
| J1P9 | All other beta-lactam antibacterials |
| J1X | OTHER ANTIBACTERIALS |
| J1X1 | Glycopeptide antibacterials |
| J1X2 | Polymyxins |
| J1X9 | All other antibacterials |

## Appendix 8. Retrieved IMS-DA Read code recoded into new four diagnostic categories

| Diagnosis Category | Diagnosis |
|---|---|
| **Upper UTIs** | Acute pyelonephritis |
| | Pyelonephritis unspecified |
| | Chronic pyelonephritis |
| | Chronic obstructive pyelonephritis |
| | Pyonephrosis unspecified |
| | Pyelonephritis unspecif.NOS |
| | Acute pyelonephritis NOS |
| **Lower UTIs** | Cystitis |
| | Acute cystitis |
| | Chronic interstitial cystitis |
| | Recurrent cystitis |
| | Chronic cystitis unspecified |
| | Cystitis NOS |
| | Cystitis cystica |
| | Other chronic cystitis |
| **UTIs** | Urinary tract infect.unsp.site |
| | Recurrent urinary tract infecn |
| | Urinary tract infection |
| | Urinary tract infect.unsp.NOS |
| | H/O: recurrent UTI |
| | Chronic urinary tract infectn |
| | Post-operative UTI |
| **Others** | Infections of kidney |
| | Bacteriuria,site not specified |
| | Pyuria, site not specified |
| | Perinephric abscess |
| | Acute pyelitis |
| | Renal abscess |
| | Renal and perinephric abscess |
| | Pyelitis unspecified |
| | Infection of kidney NOS |

# Appendix 9. Email response from the Research Ethics office at King's College London regarding DUR study ethical approval

**From:** Fieulleteau, Catherine
**Sent:** 17 July 2013 08:59
**To:** Jones, Susan
**Subject:** RE: Modification request BDM/11/12-50

Dear Sue

If the data the student is looking at is fully anonymised/anonymous, non-sensitive, pre-existing data this does not require ethical approval from this office. Further guidance can be found here:
http://www.kcl.ac.uk/innovation/research/support/ethics/training/existingdata.aspx

Kind regards

Catherine Fieulleteau
Senior Research Ethics Officer
Research Ethics Office
King's College London
5.11 Franklin-Wilkins Building
(Waterloo Bridge Wing)
Stamford Street
London
SE1 9NH
Tel: 0207 848 4070
Email: catherine.fieulleteau@kcl.ac.uk
www.kcl.ac.uk/research/ethics

# Appendix 10. Email from IMS Health ISEAC committee with regard to DUR study research protocol and results publication approval

RE: ethical approval

MGaskin@uk.imshealth.com

Tue 6/30/2015 3:09 PM

To:Long, Paul <paul.long@kcl.ac.uk>;

Cc:JKim@uk.imshealth.com <JKim@uk.imshealth.com>; PStephens@uk.imshealth.com <PStephens@uk.imshealth.com>; Alomar, Hussain <hussain.al-omar@kcl.ac.uk>; macey.murray@ucl.ac.uk <macey.murray@ucl.ac.uk>;

1 attachment (19 KB)

ISEAC 2013 006 UTI interim response to applicants-answers.docx;

Dear Dr Long,

I confirm that the application (ref ISEAC 2013/006) was received and reviewed by the Independent Scientific and Ethical Advisory Committee. In June 2014, questions raised by the committee were sent to Hussain Al-Omar, to which he responded (see attached document for questions and answers). Following this, the committee recommended approval of the application.

I need to chase internally to arrange for an invoice to be sent to cover the review. I will let you know progress, probably next week. Apologies for the delay.

Kind regards,

Marion

**Marion Gaskin, MA (Cantab.)**
**Engagement Manager**

**Real-World Evidence Solutions**

IMS Health Ltd.
210 Pentonville Road | London, N1 9JY | Mobile: +44 (0)7710 369408

*PLEASE NOTE: This e-mail and any attachments may be confidential or privileged and is solely for the intended addressee(s). Do not share or use without IMS Health approval. If received in error, please contact the sender and delete the email and any attachments. IMS Health HQ Ltd, a company registered in the UK, registered address 210, Pentonville Road, London N1 9JY, registration number: 3614620*

# Appendix 11. Recruitment email circulated research through the assistance of the Primary Care Research Manager at Imperial College London, Department of Primary Care and Public Health

**From:** [redacted]
**Sent:** 28 November 2014 18:11
**To:** [redacted]
**Cc:** Alomar, Hussain (hussain.al-omar@kcl.ac.uk)
**Subject:** Expression of Interest: Variations in ABX prescribing for UTI

Dear colleagues,

Hussain Al-Omar is conducting a PhD study on **'Variations in GPs' views and perceptions and factors influencing GPs' antibiotics prescribing for UTIs in elderly patients in a primary care setting'**, and is keen to meet with up to 20 GPs to inform his research via 30-45min discussion. Please see trailing email below about Hussain's doctoral research interest.

Hussain would be delighted to meet with you should you have the time to fit him in your busy diary. He would of course be happy to work around your schedule and to meet you at your practice/or wherever is convenient for you.

Hussain is happy to extend £100 in Amazon vouchers as a token gesture for your time.

Please do not hesitate to contact Hussain should you have an interest in supporting his research, and should you be able to fit him in over the next couple of weeks.

N.B. for those interested to participate, please email Hussain with your age, gender, certificates, years of experience, practice site location and whether you work in a private or NHS or NHS partner surgery.

With very best wishes,
Austen

Hussain Alomar, MSc
PhD Research Student
Clinical Practice and Medication Use Group
Institute of Pharmaceutical Science
King's College London
Franklin-Wilkins Building
150 Stamford Street
London
SE1 9NH
Hussain.al-omar@kcl.ac.uk
Tel: 07721661116

# Appendix 12. Invitation email sent to selected GPs

## Invitation Email

Dear Dr [redacted]

Greetings.

My name is Hussain Alomar, a PhD student, and I am doing qualitative research with a focus on antibacterials prescribing by GPs. My research title is ‘Variations in GPs’ views and perceptions and factors influencing GPs’ antibiotics prescribing for UTIs in elderly patients in a primary care setting’ and I am trying to interview GPs for this research. GPs who meet the following inclusion criteria are welcomed to take part in this research:

- GP with a degree in medicine,
- working in any NHS or NHS partner general practice surgery in Greater London
- working as a part-time or full-time GP
- any age,
- any gender,
- any practice locations,
- any practice size,
- any contract scheme,
- any number of years or practice,
- any level of experience and training qualifications.

Exclusion criteria:

- GP working in a private general practice surgery,
- GP working in any university or college primary care centre or surgery,
- GP with a poor command of English,
- GP with poor communication skills.

I am aiming to start the interviews by 7 January 2015. The interview will take approximately one hour and will be digitally recorded. If you agree to participate, I will be happy to schedule a meeting with you according to your preference for date, time and place.

As a token gesture for GPs who support this research, I will be happy to extend £100 in the form of an Amazon gift card.

Thank you for your time and consideration.

Best regards,

Hussain Alomar, MSc
PhD Research Student
Clinical Practice and Medication Use Group
Institute of Pharmaceutical Science
King's College London
Franklin-Wilkins Building
150 Stamford Street
London
SE1 9NH
Hussain.al-omar@kcl.ac.uk
Tel: 07721661116

# Appendix 13. Information Sheet sent through email to selected GPs

## INFORMATION SHEET FOR PARTICIPANTS

**YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET**

**Title of Study: Variations in GPs' views and perceptions and factors influencing GPs' antibiotics prescribing for UTIs in elderly patients in a primary care setting**

**Invitation**

I invite you to participate in this study, which will form part of my PhD research at the Institute of Pharmaceutical Science, King's College London. You should participate only if you want to; choosing not to participate will not disadvantage you in any way. Before you decide whether you want to participate, it is important for you to understand why the study is being done and what your participation will involve. Please take the time to read the following Information Sheet carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information.

**What is the purpose of the study?**

The purpose of this study is to explore the variations in the ways GPs experience, conceptualise, perceive and understand antibiotics prescribing practice for elderly patients with UTIs.

**Why have I been invited to take part?**

You have been invited to participate in this study because you are a GP working in a primary care setting and I believe that your experience and qualifications as a GP can contribute much to the understanding and knowledge of this phenomenon regarding elderly patients with UTIs.

**Do I have to take part?**

Your participation in this study is entirely voluntary. You may refuse to participate without providing any reasons and this will not disadvantage you in any way. You may choose to ask for independent information or advice about your rights as a participant or about being involved in this particular study by discussing it with others if you wish.

If you decide to participate, you will be given this Information Sheet to keep and asked to sign a Consent Form. You may also withdraw your data from the study at any time before 28 February

2015. You may also refuse to answer some or all of the questions if you do not feel comfortable with them. You should not agree to take part in this research until you have had all your questions answered satisfactorily.

**What will happen to me if I take part?**

If you decide to participate in this study, you will be given this Information Sheet to keep and asked to sign a Consent Form. The researcher will then contact you to discuss the details of the study and the interview process, schedule the interview at a time that is convenient for you and answer your questions. The interview will take place at your practice site, at any comfortable place of your choice or at King's College London, Franklin-Wilkins Building, 150 Stamford Street, London, UK, whichever is most convenient for you.

The interview will last approximately 1 hour and will be based on the interview topic guide, although it is designed to be flexible. If you do not wish to answer any of the questions during the interview, you may say so and the researcher will move on to the next question. The questions will revolve around general prescribing practice, antibacterial prescribing practice with a focus on elderly patients with UTIs and antibacterial guidelines, recommendations and decision support tools, to improve antibacterial prescribing practice. The questions will be straightforward and simple, asking what, how and why? You will then be asked to answer questions about your demographics information, educational background, qualifications and practice. The researchers will talk with you about such phenomenon in a sensitive, non-judgemental and empathic way.

The entire interviews will be digitally recorded, but participants will not be identified by name. The recorded interviews will be kept on password-locked and encrypted computer files and locked filing cabinets in the researcher's office at the Institute of Pharmaceutical Science, King's College London, Franklin-Wilkins Building, 150 Stamford Street, London, UK, until the study is finished. The information recorded is confidential, and no one else except the researcher and his research supervisors will have access to the digitally recorded interviews or transcripts. All of the digitally recorded interviews and transcripts will be deleted after completing the PhD research. If you change your mind and decide that you no longer want to take part, you may withdraw your data from the study at any time before 28 February 2015. You will not have to give a reason for your withdrawal.

**What will happen if I participate in the study but then I want to withdraw from the study?**

Participants can withdraw from the study/withdraw their data at any time without having to justify their decision. If you decide to withdraw from the study it must be before 28 February 2015. All of your information, recorded interview and data will be deleted.

**Incentives**

There will be an incentive of £100 payable as an Amazon gift card. This gift card will be given only to those who complete the interview successfully and do not withdraw from the study. This incentive is given as reimbursement for participants' time lost to take part in this study. The gift card will be distributed by the end of the study.

**What are the possible disadvantages or risks of taking part?**

There are no expected risks of participating in the study. However, the main disadvantage in participating in this study is that you will be spending approximately an hour of your time being interviewed. Some of the interview questions might cause psychological distress, anxiety or might be challenging. However, if you feel the questions are challenging and/or distressing or you feel uncomfortable, you can refuse to answer them and the researcher will move to the next question.

**What are the possible benefits of taking part?**

There are no direct benefits of your participation in this study. However, the information I get from the research will help to improve the quality of antibacterial prescribing for older people. This improvement will be noticed in the form of improving patients' outcomes, decreasing antibacterial resistance and reducing economic expenditure on all levels. Furthermore, if you like, a copy of the study findings can be sent to you by the end of the study.

**Will my taking part be kept confidential?**

All the data and information collected about you during the study will be kept strictly confidential. All information gathered within the interviews will be held on password-locked and encrypted computer files and locked filing cabinets in the researcher's office at the Institute of Pharmaceutical Science, King's College London, Franklin-Wilkins Building, 150 Stamford Street. Your information and interview will not be shared with or given to anyone except the research supervisors. At all times there will be no possibility of you as individuals being linked with the data. All recordings of data on the digital recorder and transcripts will be deleted after the PhD research is completed.

The data will be collected and stored in accordance with the UK Data Protection Act (1998), secured and encrypted against unauthorised access.

**What will happen to the results of the study?**

The results and findings from this research will be part of the researcher's PhD thesis, disseminated through scientific publications, conferences and seminars. If you like, a copy of the study results can be sent to you once the study is completed.

**Who should I contact for further information?**

If you have any questions or require more information about this research, please contact me or my research supervisors using the following contact details:

Mr Hussain Alomar
PhD Research Student
Clinical Practice and Medication Use Group
Institute of Pharmaceutical Science
King's College London
Franklin-Wilkins Building
150 Stamford Street
London
SE1 9NH
hussain.al-omar@kcl.ac.uk
Tel: 07721661116

Dr Paul Long
Reader in Pharmacognosy
5th Floor
Institute of Pharmaceutical Science
King's College London
Franklin-Wilkins Building
150 Stamford Street
London SE1 9NH
paul.long@kcl.ac.uk
Tel: 02078484842

Dr Sue C Jones
Visiting Clinical Pharmacy Practice Lecturer
Room 5.82
Department of Pharmacy
King's College London,
Franklin-Wilkins Building
150 Stamford Street,
London
SE1 9NH
sue.jones@kcl.ac.uk

**What if I have further questions, or if something goes wrong?**

If this study has harmed you in any way or if you wish to make a complaint about the conduct of the study you can contact my supervisors at King's College London using the details below for further advice and information:

Dr Paul Long
Reader in Pharmacognosy
5th Floor
Institute of Pharmaceutical Science
King's College London
Franklin-Wilkins Building
150 Stamford Street
London SE1 9NH
paul.long@kcl.ac.uk
Tel: 02078484842

Dr Sue C Jones
Visiting Clinical Pharmacy Practice Lecturer
Room 5.82
Department of Pharmacy
King's College London,
Franklin-Wilkins Building
150 Stamford Street,
London
SE1 9NH
sue.jones@kcl.ac.uk

**Thank you for reading this Information Sheet and for considering taking part in this research.**

# Appendix 14. Interview topic guide and GP demographic information

GP code:

**Variations in GPs' views and perceptions and factors influencing GPs' antibiotics prescribing for UTIs in elderly patients in a primary care setting**

**Interview introduction**

Thank you for agreeing to participate in this interview. My name is Hussain Alomar, I am a pharmacist by background, and I am a PhD research student at the Institute of Pharmaceutical Science, King's College London.

Before I start this interview, I would like to give you an overview of what I am trying to achieve. I am undertaking a service evaluation regarding antibiotics prescribing by general practitioners (GPs) with a focus on urinary tract infections (UTIs) in elderly patients in primary care. My aim is to describe the variations in the ways GPs experience, conceptualise, perceive and understand antibiotics prescribing practice. To achieve this, I am aiming to interview GPs working in primary care in London from different practice sites, with different levels of experience and different training qualifications. The interview will last for approximately one hour and will be based on an interview topic guide, although it is designed to be flexible.

In this interview, I would like to explore three main areas:

1. general prescribing practice;
2. antibiotics prescribing practice with a focus on elderly patients with UTIs; and
3. antibiotics guidelines, recommendations and decision support tools, to improve antibiotics prescribing practice.

As we agreed when I first contacted you, I will be recording the interview on a digital recorder as it will be transcribed along with others in the study. At the same time as I am recording the interview, I will take notes without distracting you from your answers. During the interview, you will have the liberty to express your perceptions, conceptions and understanding since there are no 'right' or 'wrong' answers. Depending on your responses, these questions may be followed by other probing, prompting questions. If you do not wish to answer any of the questions during the interview, you may say so and I will move on to the next question. The questions will be straightforward and simple, asking what, how and why? You will then be asked to answer questions about your demographic information, educational background, qualifications and practice.

1

What is said during the interview will remain strictly confidential as per the National Research Ethics Service (NRES) guidelines. The interview data will be encrypted and held securely in my office at King's College London, Franklin-Wilkins Building, 150 Stamford Street until the study is finished. All your information and data will be anonymised and I will refer to your information in data collection as (GPX) where X refers to your number in the study. The given code and number in relation to your information will be kept strictly confidential from everybody except my supervisors and me. In reporting the study findings, any information used or quoted from your interview will appear in the findings with reference to you as (GPX) instead of your name. At all times there will be no possibility of you as an individual being linked with the data or the findings. Your information and interview will not be shared with or given to anyone except my supervisors. The results and findings from this study will be part of my PhD thesis, disseminated through scientific publications, conferences and seminars, and, if you would like, a copy of the study findings can be sent to you.

The UK Data Protection Act (1998) will apply to all information gathered within the interview and all recorded interviews will be encrypted and held on a password-protected computer with interview transcripts locked in a filing cabinet in my office at King's College London, Franklin-Wilkins Building, 150 Stamford Street.

**Is that still OK with you?**

**Before we start, do you have any questions about the study?**

**2**

**Probing and Prompting**
**Could you explain that further? Could you please give me an example? What do you mean by that? Can you tell me more about that? Can you explain that in a different way? Is there anything else you would like to say about this?**

## PART A: INTERVIEW CORE QUESTIONS

**General prescribing practice questions:**

1. I would like to start with a very general question: in your daily practice how do you plan a clinical decision for a patient?
2. Could you describe for me the exact process you follow when you decide to prescribe a medication?
3. How have your perceptions and practice regarding clinical decision making and medications prescribing changed since you graduated from medical school? Why do you think these changes occurred?
4. How do you keep yourself up to date regarding medications prescribing and decision making?
5. Considering physicians' perspectives, in your opinion, what are the most important factors that influence your medications prescribing decisions, actions, habits and judgement?
6. Considering patients' perspectives, in your opinion, what are the factors that you believe can affect or influence your medications prescribing decisions, actions, habits and judgement?
7. Considering the healthcare system's perspectives, in your opinion, what are the factors that you believe can affect or influence your medications prescribing decisions, actions, habits and judgement?
8. Considering society's perspectives, in your opinion, what are the factors that you believe can affect or influence your medications prescribing decisions, actions, habits and judgement?
9. Which classes of medication do you believe you prescribe most often?

**Probing and Prompting**
**Could you explain that further? Could you please give me an example? What do you mean by that? Can you tell me more about that? Can you explain that in a different way? Is there anything else you would like to say about this?**

**Antibiotics prescribing practice with a focus on elderly patients with UTIs questions:**

1. What are your perceptions of antibiotic agents as medications?
2. How have your perceptions and practice regarding clinical decision making and antibiotic medications prescribing changed since you graduated from medical school? Why do you think these changes occurred?
3. What are your views regarding antibiotic prescribing appropriateness and utilisation among GPs in primary care in general? Are there any differences in the case of elderly patients with UTIs?
4. To what extent do you believe there are variations in antibiotic prescribing among GPs in a primary care setting in general? What are the reason(s) for this phenomenon? Are there any differences in the case of elderly patients with UTIs?
5. To what extent do you believe there are challenge(s) and/or problem(s) with antibiotic prescribing within primary care in general? Are there any differences in the case of elderly patients with UTIs?
6. In your view, what would help to promote the prudent utilisation and prescribing of antibiotic medications in primary care? Are there any differences in the case of elderly patients with UTIs?
7. When you plan to prescribe an antibiotic medication for a patient, what kind of references do you use or consider to support your decision? Are there any differences in the case of elderly patients with UTIs?
8. Could you describe for me the exact process you follow when you decide to prescribe antibiotic medications for your patients? Are there any differences in the case of elderly patients with UTIs?
9. How do you view your own antibiotic medications prescribing pattern and practice as compared to your colleagues' in general? Are there any differences in the case of elderly patients with UTIs?
10. How does your antibiotic medications prescribing for elderly patients differ from other age groups in general? Are there any differences in the case of elderly patients with UTIs?
11. What are the factors that influence your decision to treat an elderly patient with UTIs with antibiotic medication?
12. How does your antibiotic medications prescribing differ for old men versus old women diagnosed with UTIs?
13. Considering physicians' perspectives, in your opinion, what are the factors that you believe can affect or influence your antibiotic prescribing decisions, actions, habits and judgement? Are there any differences in the case of elderly patients with UTIs?
14. Considering patients' perspectives, in your opinion, what are the factors that you believe can affect or influence your antibiotic prescribing decisions, actions, habits and judgement? Are there any differences in the case of elderly patients with UTIs?
15. Considering the healthcare system's perspectives, in your opinion, what are the factors that you believe can affect or influence your antibiotic prescribing decisions, actions, habits and judgement? Are there any differences in the case of elderly patients with UTIs?
16. Considering society's perspectives, in your opinion, what are the factors that you believe can affect or influence your antibiotic prescribing decisions, actions, habits and judgement? Are there any differences in the case of elderly patients with UTIs?

| **Probing and Prompting** |
|---|
| **Could you explain that further? Could you please give me an example? What do you mean by that? Can you tell me more about that? Can you explain that in a different way? Is there anything else you would like to say about this?** |

| **Antibiotics guidelines, recommendations and decision support tools, to improve antibiotics prescribing practice questions:** |
|---|
| 1. In your daily practice, how often do you use and follow the antibiotics recommendations and/or guidelines? In relation to your colleagues?<br>2. How do you keep yourself up to date regarding antibiotics recommendations and/or guidelines in general? Are there any differences in elderly patients with UTIs?<br>3. Are you aware of any therapeutic recommendations and/or guidelines for the treatment of elderly patients with UTIs in a primary care setting? If yes, then which ones and when was the last time you reviewed them? Do you use and follow them in your daily practice?<br>4. In your view, what do you believe to be the gaps, factors or barriers that are influencing GPs' adherence to antibiotics recommendations and/or guidelines? Are there any differences in the case of elderly patients with UTIs?<br>5. In your view, what could be the most effective intervention(s) to improve antibiotics prescribing practice in a primary care setting? Are there any differences in the case of elderly patients with UTIs?<br>6. In your view, what could be the most effective method(s) to implement this/these intervention(s) in a primary care setting? Are there any differences in the case of elderly patients with UTIs?<br>7. In your practice, do you use any antibiotics decision support method(s), tool(s) or system to assist you in your antibiotics prescribing decisions? If yes, what is/are it/they? How often do you use it/them in your daily practice? In relation to your colleagues?<br>8. What are your views, thoughts and ideas about computerised antibiotics decision support systems as compared to other interventions in improving GPs' antibiotics prescribing practice?<br>9. Is there anything else you think I have missed in this interview that you would like to add? |

GP code:

**PART B: GP's DEMOGRAPHIC INFORMATION**

1- Gender: ☐ Female ☐ Male ☐ Other

2- Age: years

3- Primary care practice site:

4- Position: ☐ GP ☐ GP registrar ☐ Other, please specify_______________

5- Can you identify your country of study?

6- Can you identify your qualifications?

7- Can you identify your area of specialisation?

8- For how many years have you been practising as a GP?

9- Have you practised outside the UK? ☐ Yes, (Country: Duration: ) ☐ No

10- Can you identify your working pattern since you qualified as a GP (Full-time, Part-time, Weekends, Shifts, Locum)?

11- Have you changed your work pattern over the years?

12- Have you ever practised in a hospital since your graduation? ☐ Yes, (Duration: ) ☐ No

13- How many days you work per week?

14- How many patients do you see on average per day?

15- What is the average duration for each session/patient?

## Appendix 15. The result from NRES online decision tool regarding ethical requirement for qualitative research



Go straight to content.

NHS
Health Research Authority

MRC Medical Research Council

**Do I need NHS REC approval?**

This decision tool suggests that you do not need NHS REC approval, however, you may still require another type of ethics committee review, e.g. Higher Education Institutions (HEIs) ethical approval.

Researchers in HEIs are advised to check whether, under their institution's policy and internal arrangements, ethical review is required by their HEI research ethics committee.

Exceptionally, the Research Ethics Service may accept an application for review of research at the request of the **sponsor**, **chief investigator** or host organisation, where it agrees that the proposal raises material ethical issues. Agreement should be sought from the responsible operational manager for the local REC centre prior to submission of the application.

Requests should be sent by email, including a summary of the research proposal (maximum one page) and explanation of why the project raises significant issues which cannot be managed routinely in accordance with established guidelines and good practice, and requires ethical consideration and advice from an NHS REC. Contact points for operational managers can be found on the **HRA website**.

Researchers requiring further advice (e.g. those not confident with the outcome of this tool) should contact their R&D office or sponsor in the first instance, or the HRA to discuss your study. If contacting the HRA for advice, do this by sending an outline of the project (maximum one page), summarising its purpose, methodology, type of participant and planned location as well as a copy of the previous results page and a summary of the aspects of the decision(s) that you need further advice on to the HRA Queries Line at **HRA.Queries@nhs.net**.

**Follow this link to start again.**

**About this tool** **Feedback** **Contact** **Glossary**

## Appendix 16. Consent form signed by all GPs

**CONSENT FORM FOR PARTICIPANTS IN STUDY**

**Title of Study: Variations in GPs' views and perceptions and factors influencing GPs' antibiotics prescribing for UTIs in elderly patients in a primary care setting**

Thank you for considering participation in this study. The person conducting the research must explain the study to you before you agree to participate. If you have any questions arising from the Information Sheet, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

**Please tick or initial**

I confirm that I understand that by ticking/initialling each box I am consenting to this element of the study. I understand that it will be assumed that un-ticked/initialled boxes mean that I DO NOT consent to participate in this study. I understand that by not giving consent for any one element I may be deemed ineligible for the study. ☐

**Please tick or initial**

1- I confirm that I have read and understood the Information Sheet for the above study. I have had the opportunity to consider the information and to ask questions, which have been answered satisfactorily. ☐

2- I understand that my participation is entirely voluntary and that I am free to withdraw at any time without giving any reason. Furthermore, I understand that I will be able to withdraw my data up to 28 February 2015. ☐

3- I consent to the processing of my personal information for the purposes explained to me. I understand that such information will be handled in accordance with the terms of the UK Data Protection Act (1998). ☐

4- I understand that my information may be subject to review by responsible individuals from the College for monitoring and audit purposes. ☐

5- I understand that confidentiality and anonymity will be maintained and it will not be possible to identify me in any publications. ☐

6- I agree to be contacted in the future by King's College London researchers who would like to invite me to participate in follow-up studies to this research. ☐

7- I agree that the research team may use my anonymised data for future research and I understand that any such use of identifiable data would be reviewed and approved by a research ethics committee. ☐

8- I understand that the information I have submitted will be part of a PhD thesis, published in scientific journals and presented at conferences and symposiums. ☐

9- I consent to my interview being digitally recorded. ☐

1

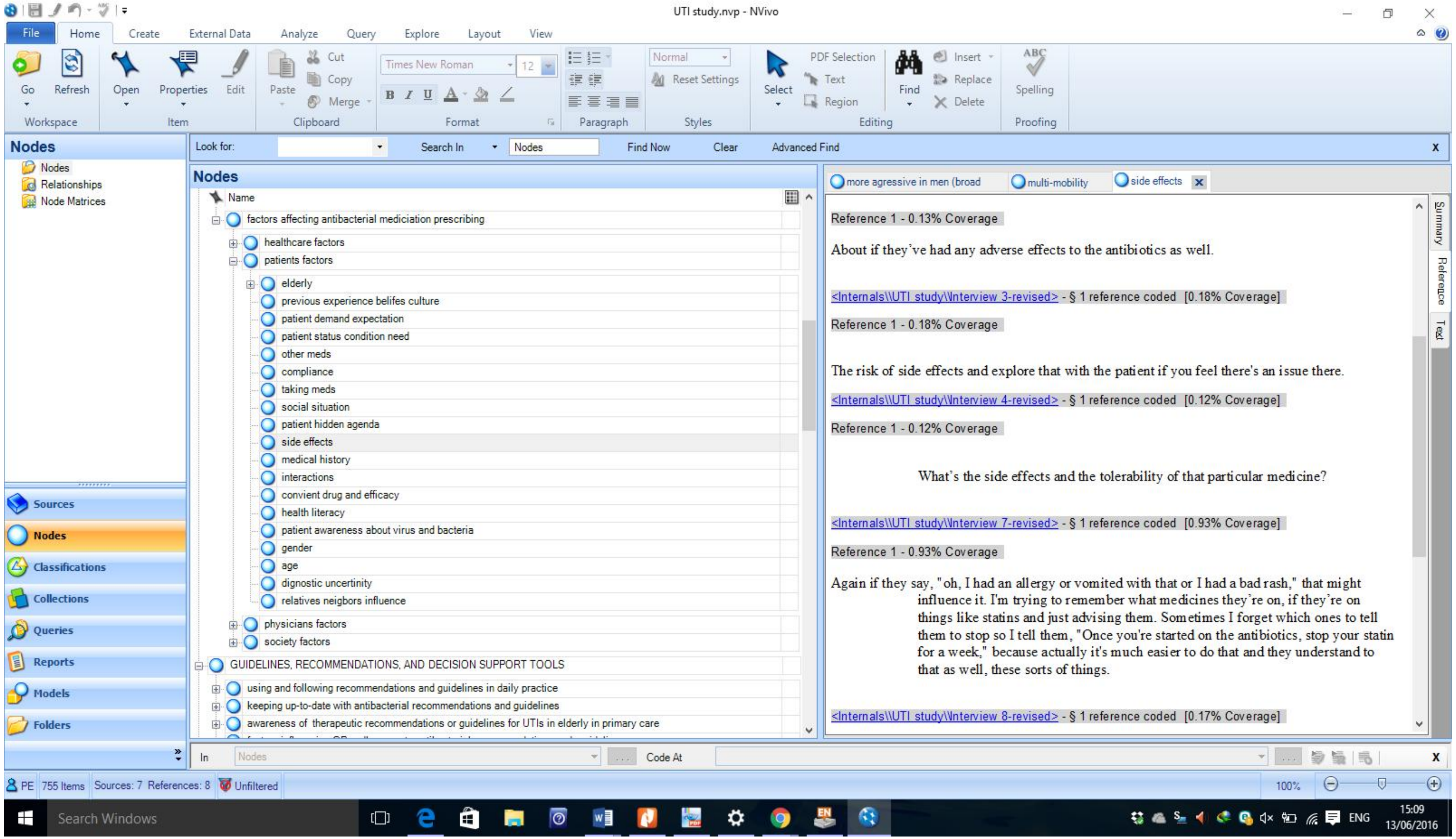
KING'S College LONDON

10- I understand that anonymised extracts from my interview may be quoted in the PhD thesis and any subsequent publications, presentations, conferences and symposiums. ☐

| | | |
|---|---|---|
| ___________________ | ___________________ | ___________________ |
| Name of Participant | Date | Signature |
| ___________________ | ___________________ | ___________________ |
| Name of Researcher | Date | Signature |

2

# Appendix 17. Example of coding GPs interviews using NVivo®



**Appendix 18. Detailed numbers on individual patient visits per age group by year and over the study period**

| Age (years) | Number of Visits per individual patient | 2010 | | 2011 | | 2012 | | Over study period | |
|---|---|---|---|---|---|---|---|---|---|
| | | N | % | N | % | N | % | N | % |
| **65-74** | **1 visit** | 1,991 | 67 | 1,853 | 64.6 | 1,588 | 63.8 | 3,928 | 59.8 |
| | **2 visits** | 524 | 17.6 | 576 | 20.1 | 482 | 19.4 | 1,211 | 18.4 |
| | **≥3 Visits** | 456 | 15.3 | 440 | 15.3 | 418 | 16.8 | 1,429 | 21.8 |
| **75-84** | **1 visit** | 1,886 | 63.6 | 1,696 | 64.9 | 1,481 | 64 | 3,532 | 53.8 |
| | **2 visits** | 550 | 18.6 | 480 | 18.4 | 432 | 18.7 | 1,106 | 16.8 |
| | **≥3 Visits** | 528 | 17.8 | 438 | 16.8 | 401 | 17.3 | 1,938 | 29.5 |
| **≥85** | **1 visit** | 1,220 | 64.7 | 1,159 | 64 | 992 | 61.9 | 2,406 | 36.6 |
| | **2 visits** | 345 | 18.3 | 315 | 17.4 | 325 | 20.3 | 714 | 10.9 |
| | **≥3 Visits** | 322 | 17.1 | 337 | 18.6 | 285 | 17.8 | 3450 | 52.5 |

**Appendix 19. Detailed numbers of antibiotics prescribed by GPs by year and over the study period**

| | 2010 | | 2011 | | 2012 | | | Over study period | |
|---|---|---|---|---|---|---|---|---|---|
| **Antimicrobial** | **N** | **%** | **N** | **%** | **N** | **%** | ***p* - value** | **N** | **%** |
| **Trimethoprim** | 5,826 | 43 | 5,245 | 40.8 | 4,701 | 41.2 | 0.68 | 15,772 | 41.7 |
| **Nitrofurantoin** | 2,892 | 21.3 | 3,324 | 25.9 | 3,232 | 28.3 | 0.11 | 9,448 | 25 |
| **Cefalexin** | 2,047 | 15.1 | 1,725 | 13.4 | 1,270 | 11.1 | 0.06 | 5,042 | 13.3 |
| **Co-amoxiclav** | 822 | 6.1 | 767 | 6 | 761 | 6.7 | 0.42 | 2,350 | 6.2 |
| **Ciprofloxacin** | 717 | 5.3 | 647 | 5 | 556 | 4.9 | 0.18 | 1,920 | 5.1 |
| **Amoxicillin** | 660 | 4.9 | 645 | 5 | 561 | 4.9 | 0.99 | 1,866 | 4.9 |
| **Others** | 587 | 4.33 | 496 | 3.86 | 334 | 2.93 | 0.04 | 1,417 | 3.7 |